

IN VIVO X-RAY FLUORESCENCE ANALYSIS

**A new technique for lead and cadmium determination
in occupationally exposed persons**

Lars Ahlgren

Lund 1980

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IN VIVO X-RAY FLUORESCENCE ANALYSIS

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Measurements on five occupationally exposed persons have shown that it is possible to use X-ray fluorescence analysis for in vivo measurements of lead in the skeleton. The technique for calibrating in vivo X-ray fluorescence measurements of lead in bone tissue has been studied in detail and a two-component phantom simulating the bone and the soft tissue parts of the finger constructed. The technique has been used for in vivo measurements on 22 occupationally exposed persons. The minimum detectable concentration of lead in fingerbones was found to be around $20 \mu\text{g} \cdot \text{g}^{-1}$. The lead concentrations in their skeletons and blood were compared: the correlation was poor. The variations in lead concentrations in the skeleton have been studied in occupationally exposed persons and in samples from archaeological skeletons. The sensitivity and the minimum detectable concentration of cadmium in the kidney cortex in in vivo measurements has been studied by measurements on kidney models. The minimum detectable concentration was $20 \mu\text{g} \cdot \text{g}^{-1}$ at a skin-kidney distance of 30 mm and $40 \mu\text{g} \cdot \text{g}^{-1}$ at 40 mm. Five persons occupationally exposed were studied.

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- ACKNOWLEDGEMENTS
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This thesis is based on the following papers:

- I X-ray fluorescence analysis of lead in human skeleton in vivo
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- II An X-ray fluorescence technique for in vivo determination of
lead concentration in a bone matrix.
Phys. Med. Biol. 24, 136-145 (1979)
- III In vivo determination of lead in the skeleton following
occupational exposure
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- IV Distribution of lead in archaeological samples of Roman skeletons
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- V Cadmium in man measured in vivo by X-ray fluorescence analysis
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Preliminary reports from this work were presented at

- 1) Ninth Nordic Meeting on Clinical Physics,
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- 2) 28th Annual Conference on Applications of X-ray Analysis,
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IN VIVO X-RAY FLUORESCENCE ANALYSIS

A new technique for lead and cadmium determination in occupationally exposed persons.

1 INTRODUCTION

In 1913 Mosley (3,4) demonstrated the well-ordered relationship between atomic number and the energy of X-rays emitted when atoms are excited. The excitation can be due to X-rays, γ -rays, electrons or other charged particles. For in vivo measurements only X-rays and γ -rays can be used. A measurement of the energies and fluence rates of X-rays emitted from unknown sample thus provides information about its elemental composition and the concentration of its various elements. When X-rays and γ -rays are used for excitation, the technique is called X-ray fluorescence analysis. Using diffraction methods, this technique has been used for many years for non-destructive measurements of the elemental composition of laboratory samples.

The development of semiconductor detectors with good energy resolution and compact radionuclide photon sources with high activities in the late 1960's have made it possible to use the technique for measurements on people. Up to now, these in vivo measurements have been carried out on natural iodine in the thyroid gland (5) and on trace elements injected in the body prior to the measurements (6).

This work introduces the X-ray fluorescence technique for in vivo determinations of lead and cadmium in persons who have been contaminated by these elements in their daily work.

2 PHYSICS OF PHOTON-INDUCED FLUORESCENCE

Photons of the energies relevant to this study interact with atomic electrons via three main modes: photoelectric absorption, incoherent (Compton) scattering and coherent scattering.

An incoming photon can create a vacancy in one of the inner electron shells if the energy of the photon exceeds the binding energy of the electron shell (photoelectric absorption). If the photon energy is larger than the binding energy of the most tightly-bound shell (the K-shell), photoelectric ab-

sorption in this shell is favoured. An electron from one of the neighbouring shells can fill the vacancy, characteristic X-rays of the K-series with energies equal to the energy difference between the shells being emitted. The excitation energy of the atom can alternatively be carried away by the emission of an outer electron from the atom (Auger electron). The mass attenuation coefficients for photoelectric absorption for different photon energies in lead and cadmium are shown in figure 1.

Incoming photons can also be scattered either with energy reduction (incoherent scattering) or without energy reduction (coherent scattering). In incoherent scattering, the incident photon interacts with a single electron and suffers both a change of direction and a reduction of energy. This interaction process is the dominating one when biological samples are irradiated with photons of energies between around 40 keV and 20 MeV (8). Figure 1 shows the mass-attenuation coefficients for incoherent scattering in water and calcium for photons of various energies. The probability for incoherent scattering is proportional to the electron density of the scattering material. The electron density is almost constant for most of the elements in biological matrices, about $3 \cdot 10^{23} \text{ g}^{-1}$.

The probability for coherent (Rayleigh) scattering increases with increasing atomic number of the scattering material, and the process is more probable for incident photons of low energy (compare figure 1). Most of the coherently-scattered photons are emitted in the forward direction (9). In order to shield the detector from the primary radiation, we have to work with scattering angles between 70° and 180° and the probability for coherent scattering in this angle interval is much smaller than that for incoherent scattering.

It is possible to use various types of photon sources for the generation of characteristic X-rays. Either a radionuclide source which emits γ - or X-rays or an X-ray tube with suitable acceleration potential and filters may be used. The radiation from the X-ray tube can be used either directly for excitation or else for the generation of quasi-monoenergetic X-rays from a secondary target. An X-ray tube operated at 100 kV gives approximately $2 \cdot 10^{12}$ photons per s, sr and mA in the continuum and approximately 10^{11} photons per s, sr and mA characteristic X-rays from the anode (10). By using secondary targets, approximately 10^{11} characteristic X-rays from the target material per s, sr and mA are produced (11). For a 700 MBq

Mass attenuation coefficient

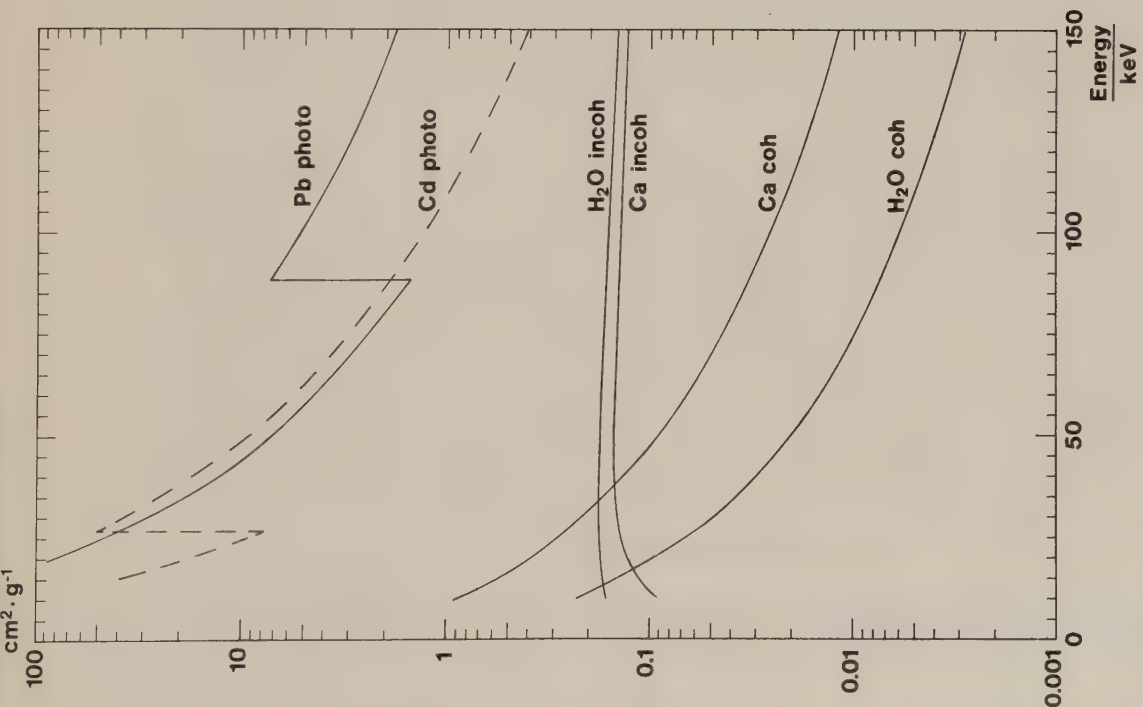


Figure 1.

The massattenuation coefficient as a function of photonenergy for photoelectric absorption in lead and cadmium, for incoherent and coherent scattering in water and calcium (7).

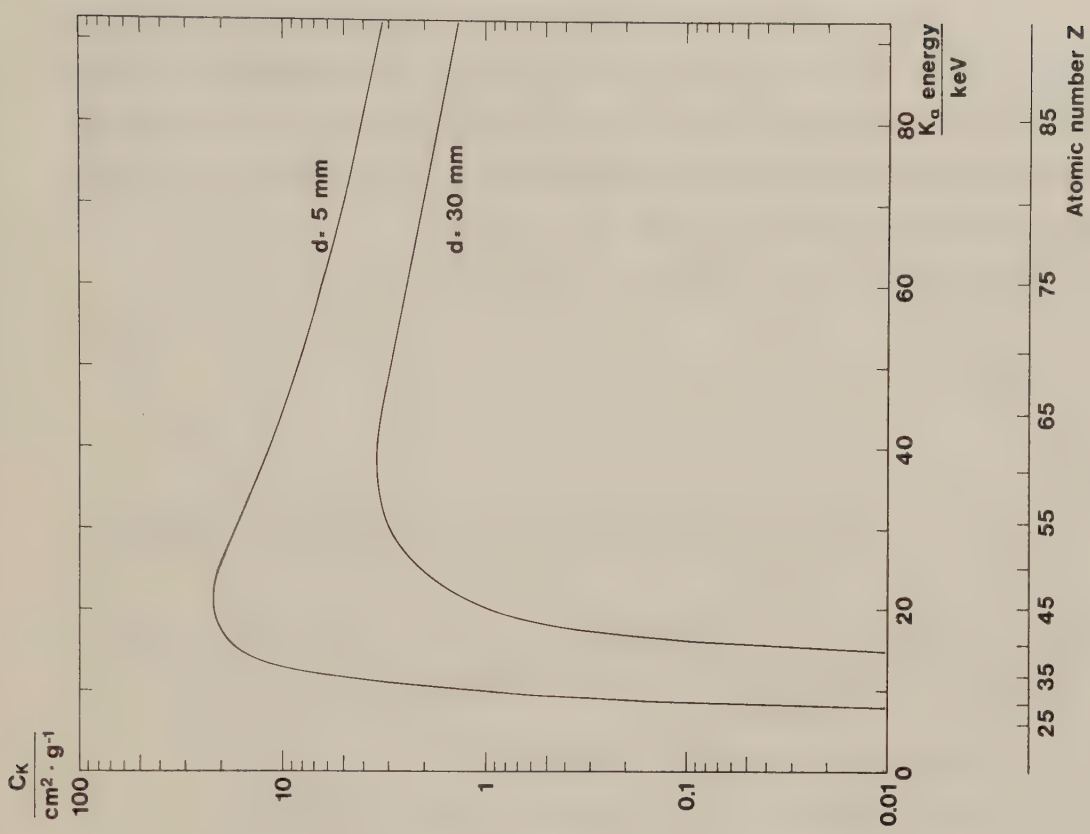


Figure 2.

Relative number of K X-ray photons, C_K , emerging from a small volume of element Z at depth d in soft tissue irradiated by photons with an energy equal to the binding energy of the K-electrons as a function of the atomic number Z.

radionuclide source emitting 1 photon per disintegration, the photon fluence rate is limited to about $6 \cdot 10^7$ per s and sr.

To get a rough idea as to which elements are available for in vivo measurements by the X-ray fluorescence technique, the fluence of characteristic K X-rays originating from a small volume located at a depth d following irradiation by photons with energies just above the binding energy of the K-electrons has been calculated.

This fluence ϕ_K is proportional to the product

$$e^{-\mu_1 \cdot d} \cdot \sigma_Z \cdot \omega_Z \cdot e^{-\mu_2 \cdot d} = C_K$$

where

μ_1 = The linear attenuation coefficient in soft tissue for incoming radiation. The energy of this radiation is taken as that of the binding energy of the K-electrons in element with atomic number Z .

σ_Z = The massattenuation coefficient for photoelectric absorption in the K-shell for element Z .

ω_Z = The K-fluorescent yield for element Z .

μ_2 = The linear attenuation coefficient in soft tissue for K_{α} X-rays from element Z .

Figure 2 shows the calculated value of C_K for in vivo X-ray fluorescence analysis of various elements and depths. As can be seen from this figure, the in vivo application of X-ray fluorescence analysis is limited to elements with atomic numbers larger than about 40. A decreasing atomic number means decreasing energy of both primary photons and characteristic X-rays. This means an increased absorption in the soft tissue layer in front of the trace element. This is not compensated for by the increasing cross section for photoelectric absorption when Z decreases below 40. In papers II and V, the minimum detectable concentrations of Pb and Cd were found to be $15 \mu\text{g} \cdot \text{g}^{-1}$ and $20 \mu\text{g} \cdot \text{g}^{-1}$ respectively. This means that elements with atomic numbers larger than 40 can be detected in concentrations of approximately $20\text{-}40 \mu\text{g} \cdot \text{g}^{-1}$ at 30 mm depth in the body and $10\text{-}20 \mu\text{g} \cdot \text{g}^{-1}$ at 5 mm depth.

3 PURPOSE OF THE PRESENT INVESTIGATION

The amount of heavy metals being handled in industries is increasing

rapidly. Some of these elements, for example, lead and cadmium, are toxic and are found to accumulate in man (12,13). There is thus considerable interest for measuring the concentrations of these elements in man and his environment.

The contamination of man by these elements is often studied by measurements on blood and urine samples. It is well-known that the lead and cadmium concentrations in such samples mainly reflects the exposure situation to which the person has been exposed recently but provides little useful information about accumulated exposures. X-ray fluorescence analysis in vivo can make it possible to measure the concentration of these elements directly in the organs which have the highest concentrations due to high uptake and/or slow excretion rates. It is possible that such information together with measurements on samples of blood and urine would provide much additional information about the behaviour and effect of these elements in man.

The purpose of the present investigation is to study the possibility of using the X-ray fluorescence technique for direct measurements of lead and cadmium concentrations in living man.

4 EXPERIMENTAL METHODS AND MATERIAL

4.1 Lead

Two different radiation sources for generation of the characteristic X-rays of lead (K_{α_1} : 75.0, K_{α_2} : 72.8 keV) have been compared, a ^{57}Co radionuclide source ($E_{\gamma} = 122.0\text{keV}$ and 136.5keV) and an X-ray tube.

The secondary radiation was studied using a 1 cm^3 Ge(Li)-detector connected via a charge-sensitivity preamplifier and a pulse-shaping linear amplifier to a 100 MHz analog-to-digital converter. A pile-up rejector and a base-line restorer were used to maintain the energy resolution at the high count rates used (up to $2 \cdot 10^4\text{ s}^{-1}$). The collimator used in front of the detector was made of high-purity tin (I,II,III) or of high purity copper covered with high purity tantalum foils (IV).

The lead concentration in the fingerbones and in some cases also the tibia of occupationally exposed persons were studied (I,III). For these measurements, two ^{57}Co radiation sources with a total activity of approximately 740 MBq were used to generate the characteristic X-rays. The count rates

of the Pb K_{α_1} and K_{α_2} X-rays were related to the lead concentration in the fingerbones by measurements on phantoms containing known amounts of lead (II) and the count rates of coherent and incoherent scattered photons was used to estimate the amount of bone mineral in the volume investigated (II,IV).

4.2 Cadmium

Two different 11 GBq ^{241}Am radiation sources ($E_{\gamma} = 59.5$ keV) were used to generate the characteristic X-rays of cadmium ($K_{\alpha} : 23.1$ keV). An annular-shaped source surrounding the detector was used in a geometry giving almost 180° between the incident and the measured radiation and a disc-shaped source was used in a 90° geometry. The minimum detectable concentration and the sensitivity for cadmium detection were studied using kidney and liver models with known amounts of cadmium. A technique for in vivo measurements of the kidney was developed with the detector at the back and the radiation source at the side of the patient giving an angle of about 110° between the incident and measured radiation. The radiation source and the detector were mounted so that they could be directed precisely towards a fixed point in the body. The technique was used to measure the cadmium concentration in the kidney of five occupationally exposed persons.

5 RESULTS AND DISCUSSION

5.1 Lead

5.1.1 Radiation sources

Figure 3 shows the pulse-height distribution from one of the ^{57}Co sources and from an X-ray fluorescence measurement of lead in water. The characteristic X-rays of lead are registered on a background mainly due to multiple scattered primary photons which limits the minimum detectable concentration. Using incident photons with energies just above the K-absorption edge (88.01 keV) and angles of $150\text{--}180^{\circ}$ between the incident and measured radiations, photons incoherently scattered in the sample towards the detector will have energies which are lower than the characteristic X-rays of lead. The registration of the characteristic X-rays will therefore be almost unaffected of the incoherently scattered photons and the probability for photoelectric absorption in the K-shell will reach a maximum. The use of a ^{109}Cd source which emits photons of energy

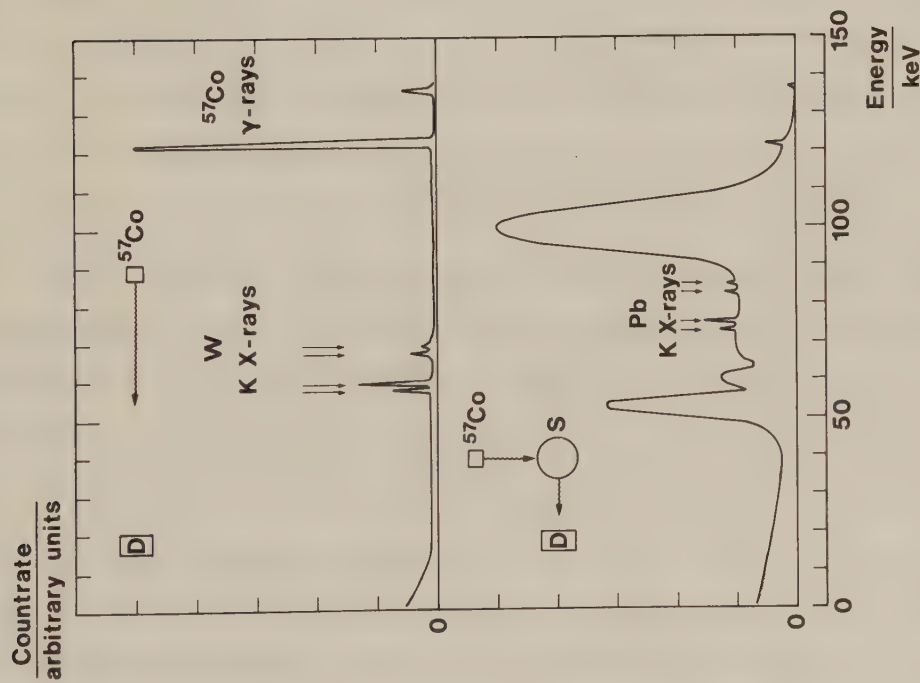


Figure 3. Pulseheight distribution from an X-ray fluorescence measurement of lead in water (bottom). The measuring geometry with the radiation source, sample (S) and the Ge(Li)-detector (D) is also shown. The pulseheight distribution from the ^{57}Co source itself is also given for comparison (top). The wolfram K X-rays arises from wolfram in the source backing.

Count rate
arbitrary units

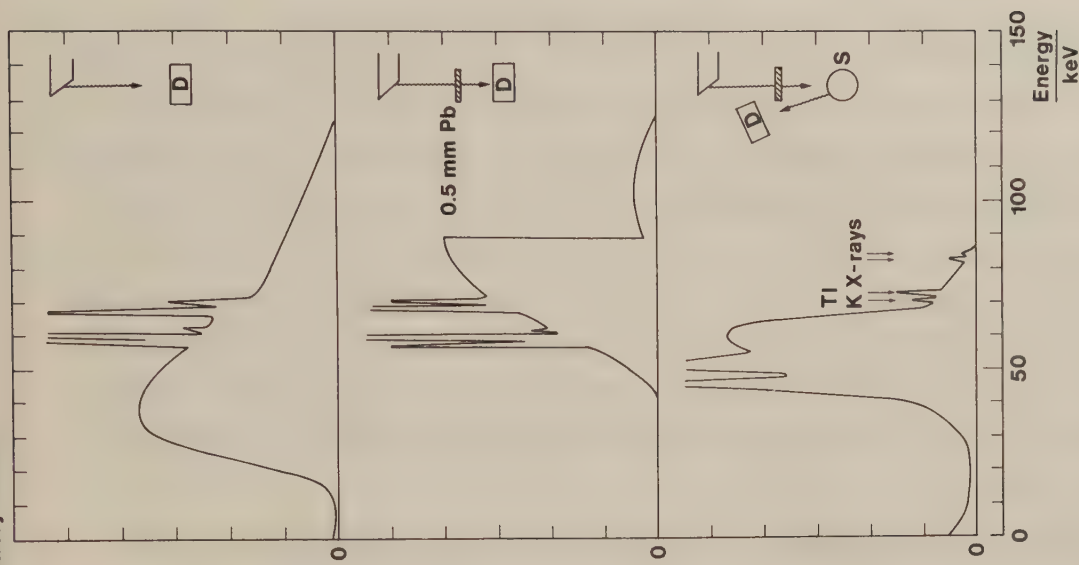


Figure 4. Pulseheight distribution from an X-ray tube with a wolfram-rhenium anode recorded in front of and behind a 0.5 mm lead filter. The pulseheight distribution from an X-ray fluorescence measurement of thallium in water and the measuring geometry, with the X-ray tube, sample (S) and the Ge(Li)-detector (D) is also shown.

88.04 keV would thus be very advantageous, but the fluence rate of the 88.04 keV photons (4% per disintegration) is too low to make the source suitable for in vivo applications at a reasonable cost.

A similar measurement geometry can also be attained using an X-ray tube with suitable filters. To study the minimum detectable concentration of lead ($Z = 82$) using a bismuth filter ($Z = 83$) in front of the X-ray tube, we determined the minimum detectable concentration of thallium ($Z = 81$) using a lead ($Z = 82$) filter in front of the tube, figure 4. The minimum detectable Tl-concentration (corresponding to a number of counts in the peak three standard deviations above the number of background counts) for the various acceleration potentials and filter thicknesses studied is compared with the detection limit reached with a ^{57}Co radionuclide source in table 1.

When the acceleration potential of the X-ray tube is increased, the numbers of useful photons increases as does the number of high energy photons penetrating the filter and increasing the background count rate in the region of interest in the pulse-height distribution. An acceleration potential of 125 kV and a 0.2 mm lead filter gave the lowest detectable concentration ($43 \mu\text{g} \cdot \text{g}^{-1}$). The limit for lead in water using a bismuth filter ($Z = 83$) may be assumed to be about the same value. The ^{57}Co source gave the lowest value of minimum detectable concentration ($12 \mu\text{g} \cdot \text{g}^{-1}$) and was chosen for the in vivo measurements.

5.1.2 Choice of measurement position

In paper I the measurements were carried out on both the tibia and the forefinger. The more extensive measurements in paper II were only carried out on the second phalanx of the forefinger. This part of the skeleton was chosen instead of the tibia since it can be held in a reproducible way close to the detector while the bone is irradiated almost uniformly. The calibration of the finger measurement is also easier to carry out since the size of the bone can be measured accurately from two X-ray pictures. The minimum detectable concentration for lead in the finger phalanx was measured to be $20 \mu\text{g} \cdot \text{g}^{-1}$ (III). The corresponding value for the tibia is higher ($40 \mu\text{g} \cdot \text{g}^{-1}$) due to an increased amount of multiply-scattered radiation in the large volume studied. The possibility that the results might have been influenced by external skin contamination is negligible since the persons studied had finished their occupationally

exposure several years prior to the measurements. Also, the skin at the measurement position was washed carefully before the measurements.

5.1.3 Efficiency for determination of lead concentrations in finger phantoms

The finger measurements in paper III were compared with measurements on phantoms consisting of two parts corresponding to the bone and the surrounding soft tissue (II). The distribution of lead in the human fingerbone is not known in detail, but the variation of the sensitivity for lead detection within the fingerbone is less than 20% in the set-up used in paper III. It is therefore an acceptable approximation to use phantoms in which the lead is homogeneously distributed. The variation in sensitivity is due mainly to the short distance between the detector and the fingerbone. The sensitivity was found to be proportional to the investigated bone volume (II) which means that the average diameter of the fingerbone must be accurately measured from X-ray pictures taken in different projections. The bone mineral concentration influences the attenuation of the primary photons and the characteristic X-rays. This effect is of minor importance because of small diameters of the fingerbones (II).

In paper I a more approximative calibration method was used. The finger measurements were compared with measurements on perspex tubes filled with lead-solution. The count rate of incoherently scattered photons was used to estimate an effective finger diameter. The lead concentration in the bone was then calculated using the ratio of Pb characteristic X-rays to incoherently scattered primary photons for perspex tubes of the effective finger diameter as discussed in paper IV. These measurements were later also compared with results from a solid two-component phantom giving approximately the same result (II).

5.1.4 Radiation dosimetry

The absorbed dose to the finger in a 40 min irradiation with the ^{57}Co sources was measured in a phantom using small LiF dosimeters (III). The maximum absorbed dose to the skin was 5.5 mGy and at the centre of the finger 2.5 mGy. When the risk for late somatic effects has to be estimated, the total energy imparted rather than the absorbed dose at a

certain point should be used. Since the total volume irradiated in a finger measurement is only about 3.5 cm^3 , the energy imparted is more than 100 times smaller than in an ordinary X-ray examination of the hand (III).

5.1.5 In vivo measurements of occupationally exposed persons

In paper I, measurements were carried out on the fingerbones and along the tibia of 5 retired metal workers who had been occupationally exposed to lead. The mean values of their lead concentration in the forefinger and tibia were 55 ± 8 and $66 \pm 5 \text{ } \mu\text{g} \cdot \text{g}^{-1}$ (± 1 S.E.) respectively. No significant difference between the measured lead concentrations in the finger and in the tibia was found. In paper III, a more extensive study of the lead concentration was carried out on 22 occupationally exposed persons of which 15 showed detectable concentrations ($\geq 20 \text{ } \mu\text{g} \cdot \text{g}^{-1}$). Figure 5 summarizes our measured lead concentrations in forefinger bones of occupationally exposed persons and the range of reported lead concentrations in the skeleton of normal individuals.

For these persons the lead concentration were found to increase with the length of employment. After approximately 30 years of occupational exposure, lead concentrations in the fingerbone were in the range $60\text{--}80 \text{ } \mu\text{g} \cdot \text{g}^{-1}$, which is in agreement with the results from paper I. This concentration is more than 10 times higher than the value for non-occupationally exposed persons from the same geographical region (15). It is of interest to compare our results for occupationally exposed persons with other in the literature. Barry and Mossman have measured the lead concentration in autopsy samples of tibia and rib from occupationally exposed persons and found mean values of 59 and $36 \text{ } \mu\text{g} \cdot \text{g}^{-1}$ respectively (17). Fleming reports "typical values" for flat bones and long bones of occupationally exposed persons of 130 and $80 \text{ } \mu\text{g} \cdot \text{g}^{-1}$ respectively (18). In bone marrow from occupationally exposed persons, lead concentrations between 42 and $350 \text{ } \mu\text{g} \cdot \text{g}^{-1}$ have been found (19). Block et al. (20) have measured the lead concentration in childrens teeth in situ to about $35 \text{ } \mu\text{g} \cdot \text{g}^{-1}$ using X-ray fluorescence analysis. Strechlow and Kneip (21) found the lead concentration in teeth to be more than 5 times the average level found in bone. Dental tissues are however normally not involved in the remodelling processes characteristic to the skeleton and both the dentine and the enamel are subject to ionic exchange with fluids in the

mouth. Teeth will therefore not necessarily reflect the lead concentration in the skeletons and thus the body burden of lead.

5.1.6 Distribution of lead in the skeleton

More than 90% of the total body burden of lead is stored in the skeleton (14, 17, 22). To be able to estimate the body burden from our in vivo measurements, it is of considerable importance to know how well the lead concentration in the fingerbones represents the average concentration in the skeleton. In paper III, we have studied the lead concentrations in different parts of the phalanx and tibia for three occupationally exposed persons. The concentrations in the three different regions of the forefinger studied were not significantly different as was not the concentration in forefinger and tibia. Concentration differences between fingerbones and tibia of up to 50% could, however, be present without being registered as significantly different.

It is not possible to carry out detailed studies of the distribution of lead in the skeletons of occupationally exposed persons by means of X-ray fluorescence measurements in vivo because of the low sensitivity in measurements on deep-lying bones. Such distribution measurements can, however, be made on autopsy samples using X-ray fluorescence analysis or, if higher sensitivity is needed, atomic absorption spectrophotometry (21). In paper IV, the distribution of lead in bone samples from four archaeological skeletons dating from a time period when the daily intake of lead was high have been studied. Measurement were carried out on samples of fingerbones as well as on samples of fibula, rib and skull and the calculated average skeleton lead concentration was expressed per mass unit of fresh weight so as to be able to compare the results with in vivo measurements (IV). In the four skeletons studied, the lead concentration in the phalanx represented the average skeleton concentration to within 50%, even if the lead concentration varied up to a factor of 4 between different bones in the skeleton (IV).

5.1.7 Dynamics of lead in blood and bone

In paper III, the lead concentrations in the skeleton and blood were compared 7 years after the occupational lead exposure had stopped. Even after this time, no simple relation between the lead concentrations in

the skeleton and blood was found. For some of these contaminated persons, the lead concentration in the blood was within the normal range indicating that the lead is firmly bound in the skeleton.

These results were used to test a two-compartment model for the kinetics of lead in the skeleton and in soft tissue. Using an average lead concentration in the skeleton of $80 \mu\text{g} \cdot \text{g}^{-1}$ as measured in the finger-bones and an estimated daily absorption of $15 \mu\text{g}$ lead from food and air, the lead concentration in the blood could be calculated to be between 0.25 and $0.40 \mu\text{g} \cdot \text{g}^{-1}$ which is in agreement with the experimentally found mean value $0.27 \mu\text{g} \cdot \text{g}^{-1}$ (III). The average lead concentration in blood for non-occupationally exposed persons from the same geographical region is $0.09 \mu\text{g} \cdot \text{g}^{-1}$. The results of paper III however indicate the necessity of carrying out measurements on the skeleton of living man to have a proper estimate of his accumulated lead exposure.

5.2 Cadmium

5.2.1 Phantom measurements

The minimum detectable concentration of cadmium was studied in a cadmium containing model of the kidney placed in water (V). Due to the attenuation of the characteristic X-rays of cadmium and the incident photons and to variations in geometrical efficiency, the minimum detectable cadmium concentration is very dependent on the thickness of the layer of tissue between the detector and the kidney surface. The minimum detectable concentration is $20 \mu\text{g} \cdot \text{g}^{-1}$ when this thickness is 30 mm and $40 \mu\text{g} \cdot \text{g}^{-1}$ when it is 40 mm , which means that the technique can be used for kidney measurements on a large group of occupationally exposed persons. Cadmium is stored mainly in the kidney cortex and due to the pronounced depth dependence of the method the measurements mainly reflect the cadmium concentration there rather than in the whole kidney (V).

The minimum detectable cadmium concentration using X-ray fluorescence analysis may be decreased using plane-polarized photons for excitation (23,24). An alternative may be to use a secondary target on an X-ray tube for excitation with the tube, the secondary target, the sample and the detector arranged in a tri-axial geometry (25).

Pb-concentration in skeleton

$\mu\text{g} \cdot \text{g}^{-1}$

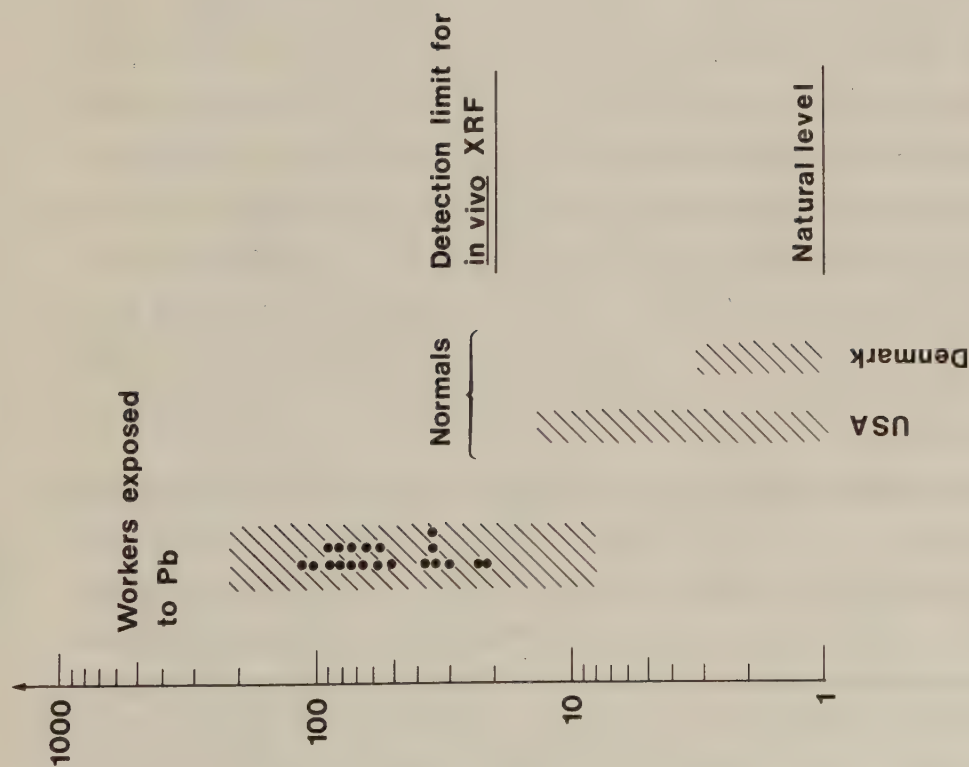


Figure 5.

The measured lead concentration in the forefinger bones of 20 occupationally exposed persons. The range of reported lead concentrations in the skeletons of occupationally (14) and non-occupationally exposed persons (14,15) as well as the estimated natural lead concentration in the skeleton (16) is also given. Our present minimum detectable concentration is indicated.

Cd-concentration in renal cortex

$\mu\text{g} \cdot \text{g}^{-1}$

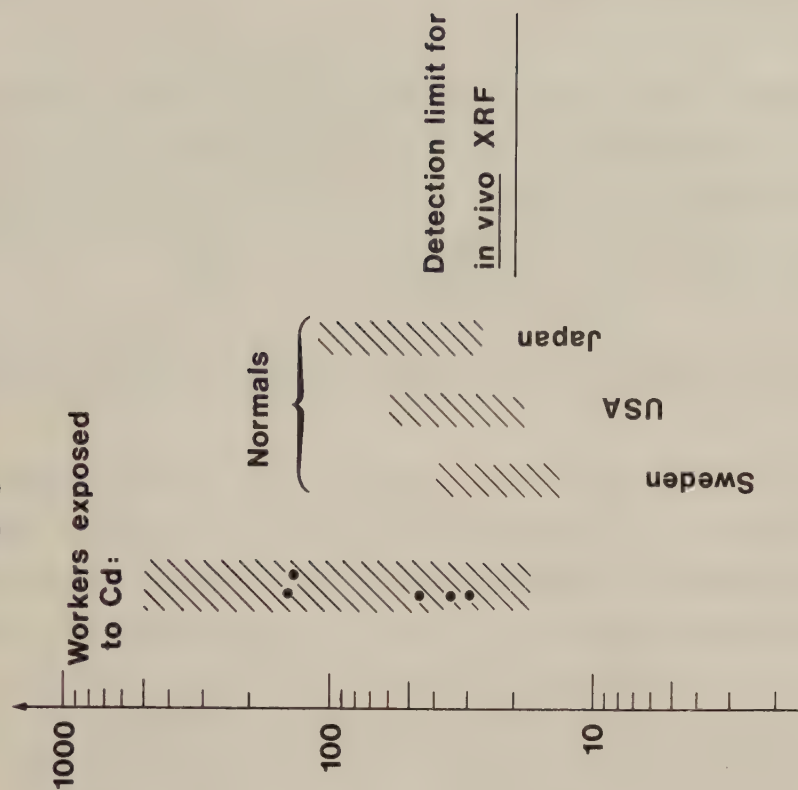


Figure 6.

The measured cadmium concentration in the kidney cortex of 5 occupationally exposed persons. The range of reported cadmium concentrations in the kidney cortex of occupationally and non-occupationally exposed persons is also given (13). Our present minimum detectable concentration is indicated.

5.2.2 Radiation dosimetry

The absorbed dose rates at different positions in a water phantom were measured with LiF dosimeters. The mean absorbed dose to the kidney was 0.6 mGy and the energy imparted was 0.4 mJ per measurement (30 min irradiation) (V). The corresponding values for a common X-ray investigation of the kidney (urography) are 3 mGy and 240 mJ (26).

5.2.3 In vivo measurements of occupationally exposed persons -----

The cadmium concentrations in the kidneys of persons who had been occupationally exposed to cadmium-containing smoke over periods from 6 to 30 years were studied in paper V. The distance between the kidney surface and the skin was measured with a B-scan ultrasonic technique. Repeated measurements of this distance showed that the standard deviation of a depth measurement was about ± 1 mm. As the kidney may move during the measurement, the total uncertainty in the distance was estimated to be ± 3 mm, giving rise to an uncertainty of $\pm 30\%$ in the calculated cadmium concentration. The cadmium concentrations in the kidney cortices of our occupationally exposed persons was found to be between 143 and $30 \mu\text{g} \cdot \text{g}^{-1}$. With one exception, the cadmium concentration increased with the period of exposure. If renal damage is present, cadmium excretion will increase and the cadmium concentration in the kidney decrease (13). This may explain why one person who had been heavily exposed for 30 years had a very low concentration in the kidney. The cadmium concentrations found in the kidney cortices of our group of occupationally exposed persons are within the range reported by Friberg et al. (13) from measurements on autopsy material from other groups of occupationally exposed persons. Figure 6 summarizes reported concentrations of cadmium in the renal cortices of occupationally exposed workers and normals and our present minimum detectable concentration.

5.2.4 Comparison with the prompt gamma neutron activation technique

In vivo measurements of cadmium have also been carried out using neutron capture γ -ray analysis (27). The kidney is irradiated with neutrons and measurements are carried out on the 559 keV γ -rays promptly emitted after the capture of slow neutrons by ^{113}Cd which constitute 12% of the total cadmium amount. Using this method, the sensitivity is

almost constant within the kidney and the detection limit is $16 \mu\text{g} \cdot \text{g}^{-1}$ for a 30 min measurement (27). In so far as patient irradiation is concerned, the X-ray fluorescence method is more favourable. Due to the small irradiated area (3 cm^2), the energy imparted is only around 0.4 mJ for the X-ray fluorescence technique compared with approximately 1.5 mJ for the neutron capture technique (V). It must also be borne in mind that the biological effects of the energy imparted by neutrons may, at low absorbed doses, be 10-100 times larger than that of the same energy imparted by photons (28).

6 SUMMARY

The contents of the papers constituting this thesis can be summarized briefly as follows.

After initial model studies measurements of five occupationally exposed persons show that it is possible to use X-ray fluorescence analysis for in vivo measurements of lead in the skeleton by using a ^{57}Co source for excitation and a Ge(Li)-detector for registration of the K X-rays (I). So far as we are aware this is the first in vivo measurement of lead in man. The technique required for calibration in vivo X-ray fluorescence measurements of lead in bone tissue has been studied in detail and a two-component bone model constructed and used to simulate the bone and the soft tissue parts of fingers (II). The minimum lead concentration detectable was around $20 \mu\text{g} \cdot \text{g}^{-1}$. The technique was used for in vivo measurements on 22 occupationally exposed persons. Lead concentrations in their skeletons and blood were compared, the correlation being found to be poor (III). The variation in the lead concentration in the skeleton has been studied in occupationally exposed persons (III) and in samples from archaeological skeletons (IV).

In the second part of the thesis the sensitivity of detection and the minimum concentration detectable in in vivo measurements of cadmium in the kidney cortex was studied by measurements on kidney models. The minimum detectable concentration was found to be $20 \mu\text{g} \cdot \text{g}^{-1}$ at a skin-kidney distance of 30 mm and $40 \mu\text{g} \cdot \text{g}^{-1}$ at 40 mm. Five persons occupationally exposed to cadmium were studied.

Table 1. The minimum detectable thallium concentration ¹⁾

Acceleration potential kV	Tube current mA	Lead filter mm	Minimum detectable Tl conc $\mu\text{g} \cdot \text{g}^{-1}$
100	5	0.50	102
125	5	0.75	63
125	5	0.50	58
125	5	0.40	50
125	5	0.30	45
125	5	0.20	43
⁵⁷ Co radionuclide source			12

¹⁾ corresponding to a number of counts in the peak which is 3 standard deviations above the number of background counts after 15 minutes measuring time.

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X-ray fluorescence analysis of lead in human skeleton in vivo

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AHLGREN, L., LIDÉN, K., MATTSSON, S. and TEJNING, S. X-ray fluorescence analysis of lead in human skeleton in vivo. *Scand. j. work environ. & health* 2 (1976) 82—86. The lead concentration in the skeleton of living man was measured by X-ray fluorescence analysis. Five former workers from a metal industry were studied. The mean lead concentration in their skeletons was estimated to be 62 $\mu\text{g/g}$ with a standard error of $\pm 5 \mu\text{g/g}$. A comparison with the "normal" skeletal concentrations of lead in people from southern Sweden showed the skeletal concentrations of the men studied to be about three to nine times higher.

Key words: X-ray fluorescence, in vivo measurements, lead, skeleton, metal industry.

X-ray fluorescence analysis is a well established technique used in determining the elemental composition of various laboratory samples. The introduction of solid state detectors with high energy resolution has made it possible to use this technique for in vivo studies (3). In in vivo studies the tissue volume is irradiated with X- or γ -radiation and the resulting characteristic X rays are measured with a Ge(Li) or a Si(Li) spectrometer. Except for the unique occurrence of a high iodine concentration in normal thyroid tissue (400—600 $\mu\text{g/g}$), the stable elements studied in living man by this technique have been administered as a tracer (2).

The present work introduces the X-ray fluorescence method for in vivo determina-

tion of the lead content in the skeleton of workers in the lead industry.

EXPERIMENTAL TECHNIQUE

A 20 mCi ^{57}Co source, mainly emitting 122 keV γ rays, was used for the generation of the characteristic X-radiation of lead. The collimator and the radiation shield consisted of high purity tin. Moreover, we eliminated the small contribution of characteristic X rays from lead impurities in the collimator by covering its opening with high purity gold.

A 16 mm (diameter) $\times$ 5.2 mm Ge(Li) detector was used (energy resolution FWHM = 750 eV at 75 keV; entrance window = 0.13 mm Be). The angle between the incident and measured radiation was 90°.

IN VIVO MEASUREMENTS

Five males were studied. They had formerly worked in a metal industry and

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Table 1. Lead concentration in five former workers from a metal industry.

Person	Age (a)	Time of employment in lead industry (a)	Time after retirement (a)	Lead concentration in blood		Lead concentration in skeleton, determined by in vivo X-ray fluorescence analysis ($\mu\text{g per g} \pm 1 \text{ SD}$)				
				Mean value during the last 5 years of employment ($\mu\text{g per g}$)	Value at the time of bone measurements ($\mu\text{g per g}$)	Forefinger		Tibia (left)		
						Right	Left	Position 1	Position 2	Position 3
ON	66	17	2	0.68	0.43	70 $\pm$ 12		46 $\pm$ 9	96 $\pm$ 13	77 $\pm$ 15
JB	71	23	4	0.65	0.41	90 $\pm$ 15		75 $\pm$ 10	84 $\pm$ 15	
MB	64	22	4	0.73	0.32	52 $\pm$ 9		70 $\pm$ 11	74 $\pm$ 12	45 $\pm$ 12
AS	67	27	1	0.63	0.51	30 $\pm$ 8	41 $\pm$ 8	51 $\pm$ 11	79 $\pm$ 17	
HLL	66	22	0.5	0.68	0.42	43 $\pm$ 7	58 $\pm$ 9	34 $\pm$ 12	55 $\pm$ 12	
Mean value (± 1 standard error)	67	22	—	0.67	0.42	55 $\pm$ 8		66 $\pm$ 5		

had handled much lead. They had retired 0.5—4 years before the measurements (table 1). During a period of several years they had shown a high lead content in their blood.

X-ray fluorescence measurements were made at three to four sites on every man, namely, on the left and/or right forefinger (fig. 1), on the tibia 8 cm from the ankle (position 1), on the tibia at about 20 cm from the ankle (position 2), and, in two cases, on the tibia at about 28 cm from the ankle (position 3).

Fig. 2 shows a typical pulse height distribution from a measurement of a forefinger. The distribution is dominated by pulses due to the Compton scattering of 122 keV (and 136 keV) photons at about 90°. One can also recognize a peak due to

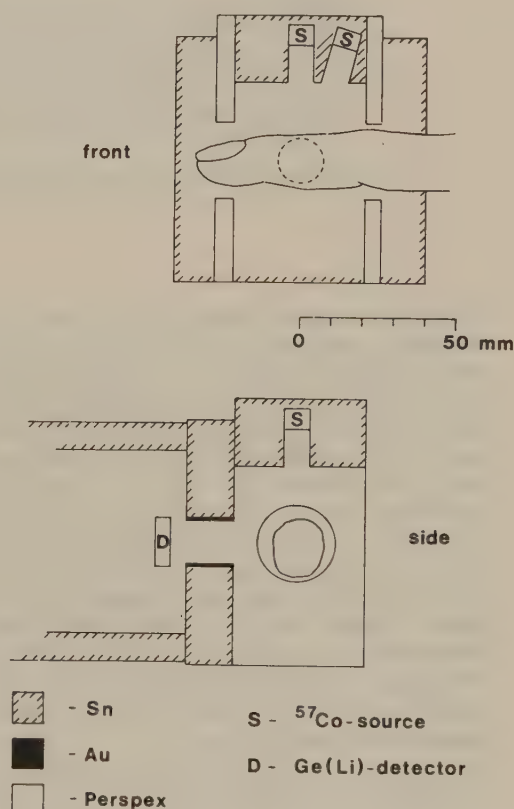


Fig. 1. Arrangement for the determination of lead in fingers by X-ray fluorescence analysis. The radiation shield, the ^{57}Co source (20 mCi), the detector-collimator with its gold-covered opening, and the Perspex holder for the finger are shown.

coherent scattering of primary photons and peaks from characteristic X rays from gold in the collimator. The small peaks from $K_{\alpha 1}$ - and $K_{\alpha 2}$ -radiation from lead in the forefinger are located in the valley between the K_{α} and K_{β} peaks from gold.

The effective registration time at each site was 15 min, but the real measurement time lasted 20–30 min because of the dead time of the multichannel analyzer.

RADIATION DOSIMETRY

In the present experiment the absorbed dose at the surface of the skin was estimated to be less than 800 mrad for a 30-min irradiation period. Since the irradiated area was very small, about 3 cm², the integral dose was insignificant in comparison with that of an ordinary X-ray examination.

RESULTS AND DISCUSSION

For all measuring sites on all five subjects a statistically significant net number of pulses was found in the $K_{\alpha 1}$ and the $K_{\alpha 2}$ regions of the registered pulse height distribution (table 2).

Measurements on finger phantoms filled with distilled water or measurements on one of the authors gave no net number of pulses in the corresponding region.

In order to estimate the lead content in the irradiated tissue seen by the detector, we measured known concentrations of lead in different phantoms for comparison.

The forefinger measurements were compared with measurements on cylindrical Perspex tubes (wall thickness = 1.5 mm) of various diameters filled with a known concentration of lead nitrate in a water solution. As expected, the counting rate in the K_{α} peaks varied considerably with tube diameter. This counting rate was proportional to the irradiated water vol-

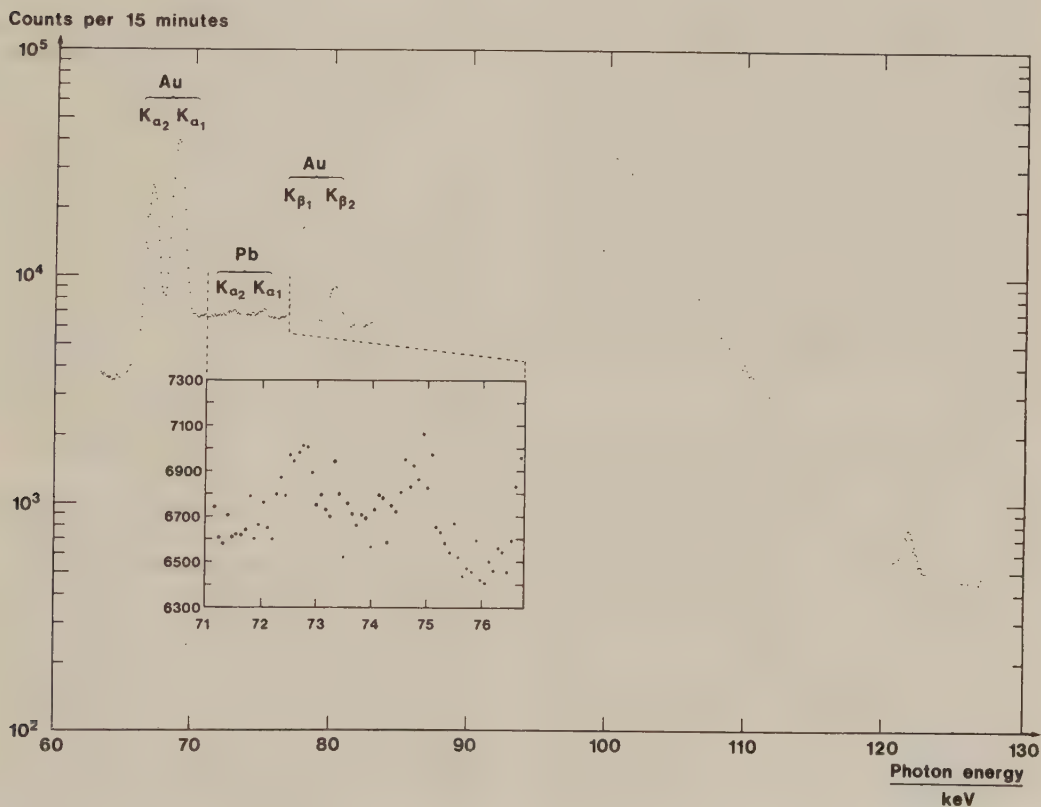


Fig. 2. Pulse height distribution recorded in an X-ray fluorescence study of the forefinger of a retired worker from the metal industry.

Table 2. Net counting rate (min⁻¹) in the Pb-K α_1 and Pb-K α_2 regions (74.97 ± 0.36 and 72.80 ± 0.36 keV).

Person	Net number of pulses per minute (± 1 SD)				
	Forefinger		Tibia		
	Right	Left	Position 1	Position 2	Position 3
ON	323 $\pm$ 33		287 $\pm$ 40	425 $\pm$ 35	251 $\pm$ 37
JB	305 $\pm$ 30		426 $\pm$ 47	278 $\pm$ 39	
MB	275 $\pm$ 34		386 $\pm$ 45	372 $\pm$ 45	186 $\pm$ 45
AS	161 $\pm$ 36	234 $\pm$ 34	251 $\pm$ 43	223 $\pm$ 36	
HL	253 $\pm$ 35	253 $\pm$ 32	145 $\pm$ 42	229 $\pm$ 42	

ume seen by the detector. For instance, if the inner diameter of the tube was increased from 15 to 25 mm, the counting rate increased by a factor of 2.4. In addition the counting rate in the Compton "peak" varied with tube diameter. If the outside diameter of the tube was increased from 15 to 25 mm, the counting rate increased by a factor of 2.2.

The number of Compton interactions is proportional to the electron density of the scattering material. As the number of electrons per mass unit is almost independent of the atomic number, the counting rate in the Compton "peak" is proportional to the mass of the volume examined. The attenuation of the incoming primary photons and the generated characteristic lead X rays is dominated by Compton interactions both in bone and in water. Therefore, as a first approximation, the ratio between the counting rates in the lead K α peaks and the Compton "peak" is dependent only on the lead concentration and is independent of the atomic number and the density of the surrounding matrix.

In the finger measurements the "effective diameter" of the finger was estimated from the counting rate in the Compton "peak" of the phantom measurements. The relationship between counting rate in the Compton "peak" and the K α peaks obtained from the finger phantom measurements was then used to estimate the concentration in the finger.

The tibia measurements were compared with measurements on cylindrical Perspex tubes filled with a known concentration of lead nitrate in a water solution and placed in a paraffin phantom. The ratio between the counting rate in the K α peaks and the Compton "peak" was studied

for the actual geometries and used for the estimation of the lead concentration in the tibia. The tibia measurements were less accurate than those of the forefinger mainly because of certain difficulties in defining the geometry. A comparison of the tibia and the finger measurements, however, strongly indicated that there could be no significant external contamination of the fingers.

Table 1 summarizes the estimated lead concentrations in the forefingers and tibia of the five persons studied. Table 1 also shows the blood lead content determined by atomic absorption spectrophotometry of blood samples obtained on the day the in vivo measurements were made. The mean value of the blood lead concentrations during the last 5 years of employment is also shown. According to table 1, on the average, no statistically significant difference in lead contamination between the forefinger and tibia was observed for the persons studied, and the individual lead concentrations did not differ significantly. The mean lead concentration determined for all the skeletal measurements, i.e., three to four sites on each of the five subjects, was 62 $\mu\text{g/g}$ with a standard error of ± 5 $\mu\text{g/g}$.

According to the unpublished results of Schütz the "normal" blood lead concentration of people from southern Sweden is between 0.05 and 0.13 $\mu\text{g/g}$. Using a ratio estimated from Barry and Mossman (1), between the concentration of lead in bone and in blood for males between 60 and 79 years of age, we found the "normal" concentration in the skeleton of people of the same age from southern Sweden to be between 7 and 18 $\mu\text{g/g}$. Therefore the five men studied in this investigation had a lead content in the studied parts of their

skeleton which was about three to nine times higher than the calculated "normal" mean value.

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An X-ray Fluorescence Technique for *in vivo* Determination of Lead Concentration in a Bone Matrix

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ABSTRACT. We have previously reported the *in vivo* detection of lead in the skeleton of man by means of X-ray fluorescence analysis using a 740 MBq ^{57}Co source for excitation and a 1 cm³ Ge(Li) detector for registration of the Pb K _{α} and K _{β} radiation. The varying geometry, density and atomic composition of the tissues of interest (mainly fingers) introduce several problems in estimation of the true concentration of a given element. A two-component cylindrical finger phantom was therefore constructed from silica paraffin wax and animal bone ash.

The diameter of the finger bone was estimated from X-ray examinations in two orthogonal projections. The bone mineral concentration was then estimated from the quotient of the number of coherent and Compton scattered primary photons. The lead concentration in the finger bones was then derived from a measurement on a finger phantom made of silica paraffin wax and bone ash with the same size and bone mineral concentration as the real bone. The minimum detectable lead concentration in a finger bone was 14 $\mu\text{g g}^{-1}$ for 15 min measuring time.

The lead concentration measured in workers from a metal industry was found to be in the range of 40-100 $\mu\text{g g}^{-1}$.

1. Introduction

An X-ray fluorescence technique using a ^{57}Co source for excitation and a Ge(Li) spectrometer for registration of the X-rays was recently developed by us to estimate the lead concentration in the skeleton of workers from a metal industry by means of *in vivo* measurements (Ahlgren, Lidén, Mattsson and Tejning 1976, Ahlgren, Lidén and Mattsson 1977). A similar technique has also been used to estimate the lead concentration in children's teeth *in situ* (Bloch, Garavaglia, Mitchell and Shapiro 1977).

A primary concern in all X-ray fluorescence analysis *in vivo* is to relate the registered net counting rate of characteristic X-rays to a proper mean concentration of the element in the tissue volume under study. Normally the anatomical structure can be described with sufficient accuracy by X-ray examination or ultrasound techniques, but the varying density and atomic number of human tissue introduce several problems in estimation of the true concentration of a given element. In this work we have studied the possibilities of simulating the properties of human soft tissue with respect to the attenuation of low energy photons by using solid phantoms of different materials. A

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technique is also described for introducing known amounts of lead into a matrix which simulates living bone. This calibration method has been used to determine the lead concentration in the skeleton of workers from a metal industry.

2. Choice of a solid material to simulate soft tissue and construction of a finger phantom

Fig. 1 shows the pulse height distribution obtained from an X-ray fluorescence measurement on a cylinder containing small amounts of lead ($200\text{ }\mu\text{g per g}$) irradiated by a ^{57}Co source in the set-up shown in fig. 2. The counting rate due to Compton scattering is proportional to the number of electrons in the volume examined. As the number of electrons per unit mass is almost the same for

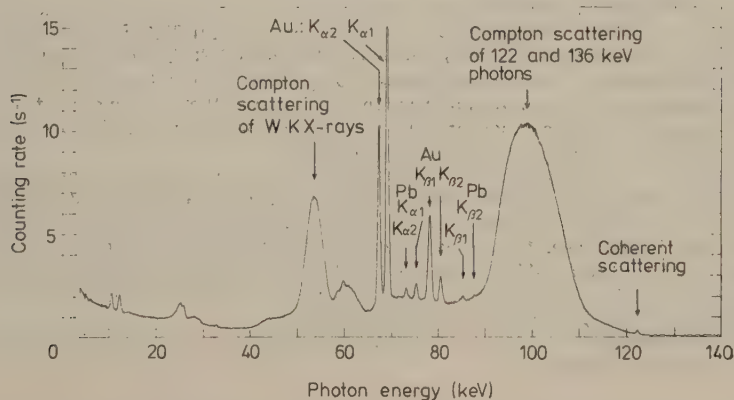


Fig. 1. Pulse height distribution from an X-ray fluorescence measurement of a homogeneous cylindrical phantom with a lead concentration of $200\text{ }\mu\text{g per g}$.

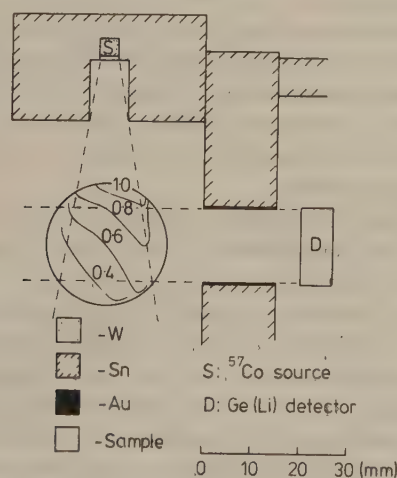


Fig. 2. The experimental set-up and the relative registration efficiency for lead in a homogeneous cylindrical phantom composed of 90% silica paraffin wax and 10% bone mineral.

muscles and bone this counting rate is proportional to the mass of the examined volume. The cross-section per atom for coherent scattering is proportional to $Z^{2.4}$ (Weber and van den Berge 1969): therefore the counting rate in this peak is related to the bone mineral concentration in the volume considered. The counting rate in the lead X-ray peaks yields information on the amount of lead in the volume under study. Thus, the pulse height distribution contains information both on the mass and the atomic composition and the amount of lead in the volume examined. The relationship between the counting rates in the peaks mentioned above can be studied to derive the lead concentration of the living bone by measurements on finger phantoms with different bone mineral concentrations and with known amounts of lead.

Water simulates soft tissue well (ICRU 1970) and the soft tissue phantom materials of potential interest have been compared to water-filled phantoms. Finger-like cylinders 50.0 mm in length and 20.0 mm in diameter were constructed of various materials and the transmission of 60 and 122 keV photons along the axis was measured relative to a water-filled phantom of the same dimensions. The measurements were carried out in a narrow beam geometry with a 1 cm³ Ge(Li) low energy photon spectrometer, for which the energy resolution (FWHM) at 75 keV was measured as 700 eV. The measured ratio of the linear attenuation coefficient for the phantom material to that of water is given in table 1. This ratio has also been calculated by means of the known element composition and published atomic cross-sections (Storm and Israel 1970). The theoretical results are in good agreement with the observations.

Measurements of the Compton and coherent scattering in the phantom material have been carried out in the geometry indicated in fig. 2. The counting rates from about 90° Compton-scattered 122 and 136 keV photons and from about 90° coherent-scattered 122 keV photons were compared to the corresponding counting rate from a water-filled phantom. The relative counting rate due to Compton scattering is in good agreement with the calculated relative cross-section for all the phantom materials investigated. However, in the case of coherent-scattered 122 keV photons the measured relative counting rate is approximately 30% higher than the calculated relative cross-section for all phantom materials except perspex and paraffin.

Mix D (Marcus 1956), silica paraffin wax (Harris, Tuddenham, Stanton, Glauser and Pendergrass 1956) and Alderson phantom material (Alderson Research Laboratories, personal communication) consist mainly of hydrocarbons. Small amounts of high Z materials are then added to enhance photoelectric absorption and coherent scattering. As the cross-sections per atom for these interactions are approximately proportional to $Z^{4.8}$ and $Z^{2.4}$ respectively (Weber and van den Berge 1969) the phantom material conceived in this manner can never be tissue-equivalent for both these interactions. It is also important that the phantom material has about the same density as tissue. Materials with higher (or lower) density cannot be compensated for by using a smaller (or bigger) phantom as this would introduce geometrical errors in the compact detector-source geometry. For perspex the density is too high and for paraffin both the density and the atomic number are too low for these

Table 1. Radiophysical properties of different phantom materials

Phantom material	Chemical composition	Measured density (g cm ⁻³)	Electron density (g ⁻¹) × 10 ²³	Measured linear attenuation coefficient relative to water		Measured counting rate relative to water	
				60 keV μ/μ _{H₂O}	122 keV μ/μ _{H₂O}	90° Compton scattered 122 and 136 keV photons	90° coherent 122 keV photons
'Soft tissue' (ICRU 1970)	0.3% K, 10.2% H, 12.3% C, 3.5% N, 72.9% O, 0.2% P, 0.5% S	1.04†	3.31	1.04‡	1.03‡	1.01§	1.01§
Water	H ₂ O	1.00	3.34	1.00	1.00	1.00	1.0
Plexiglas	(C ₅ H ₈ O ₂) _n	1.18	3.25	1.10	1.13	1.10	0.9
Polystyrene	(C ₈ H ₈ O ₂) _n	1.05	3.18	1.00	1.00	1.01	1.3
Paraffin	(CH ₃) _n	0.90	3.45	0.83	0.87	0.93	0.9
Alderson phantom material	66.7% C, 8.86% H, 21.1% O, 3.10% N, 0.16% Sb	1.03	3.27	1.01	0.99	0.99	1.3
Mix D	91.2% (CH ₂) _n , 6.4% MgO, 2.4% TiO ₂	0.97	3.41	0.98	0.97	0.99	1.4
Silica paraffin wax	81% (CH ₂) _n , 19% SiO ₂	1.02	3.37	1.05	1.02	1.02	1.4
Silica paraffin wax with 10% bone ash	73% (CH ₂) _n , 17% SiO ₂ , 10% bone ash	1.09		1.38	1.13	1.05	3.2
Silica paraffin wax with 20% bone ash	65% (CH ₂) _n , 15% SiO ₂ , 20% bone ash	1.21		1.53	1.19	1.12	5.1
Silica paraffin wax with 30% bone ash	57% (CH ₂) _n , 13% SiO ₂ , 30% bone ash	1.27		1.77	1.31	1.17	6.1

† ICRP 1975.

‡ ICRU 1970.

§ Calculated from elemental composition (ICRU 1970) and atomic cross-section (Storm and Israel 1970).

materials to be tissue-equivalent. Both polystyrene and the Alderson phantom material have good radiophysical properties, but it is difficult to alter the composition of these materials to simulate bone tissue.

Mix D, which is a commonly used phantom material, was excluded because of problems in achieving a homogeneous distribution of the MgO and TiO₂ powder in the paraffin-polyethylene mixture. Silica paraffin wax was chosen as the phantom material in this work because it is easy to handle and has acceptable radiophysical properties. It is also easy to construct a bone phantom of this material by the addition of finely ground bone ash. The finger phantoms consist of two parts, one part made of silica paraffin wax simulating the surrounding soft tissue, and the central bone-simulating part made of 70, 80 or 90% (by weight) silica paraffin wax mixed with 30, 20 or 10% finely ground bone ash (particle diameter < 0.1 mm) respectively. The relation between bone ash and soft tissue in the bone-simulating part was chosen in the interval given by the ICRP (1975) for human bone. The bone ash (575 °C) was derived from the compact part of cattle bone. The silica paraffin wax was produced by adding diatomaceous earth (19% by weight) to melting paraffin (81%) (Harris *et al.* 1956). The mixture was congealed in moulds which were then cut to the right dimension. The temperature of the melting paraffin was kept just above the melting point (57 °C) to avoid separation of the diatomaceous earth in the mixture when this congealed. Known amounts of lead were introduced in the bone simulating part by spraying lead acetate solution onto finely ground bone ash. After drying at 40 °C overnight the lead-doped powder was carefully mixed with the diatomaceous earth and poured into the melting paraffin.

3. Measurements on finger phantoms

The finger phantoms were studied by the X-ray fluorescence technique with the geometry seen in fig. 2. Each phantom was measured four times and rotated 90° between each measurement in order to check that the lead was homogeneously distributed in the bone cylinder. The calculated relative registration efficiency for lead located in various parts of a bone cylinder (90% silica paraffin wax and 10% bone ash) is given in fig. 2. This non-uniform efficiency is mainly due to the varying fluence of the primary photons and the varying solid angle of the detector arising from small distances between the radiation source, sample and detector. The varying attenuation of the photons is of less importance. The counting rate in the lead K_α peaks depends on the number of lead atoms in the irradiated volume of the bone cylinder as seen by the detector (fig. 2). This number of lead atoms can be changed by altering the lead concentration in the bone cylinder. Fig. 3 shows a linear relation between the lead K_α counting rate and the lead concentration in bone cylinders of the same diameter d and bone mineral concentration. In the blank bone cylinder no lead has been added and the counting rate in the lead K_α peaks from this bone cylinder is mainly attributed to K_α-radiation, which is generated in Pb impurities in the detector collimator by photons which are Compton-scattered in the phantom. The lead content in the blank phantom is only of minor

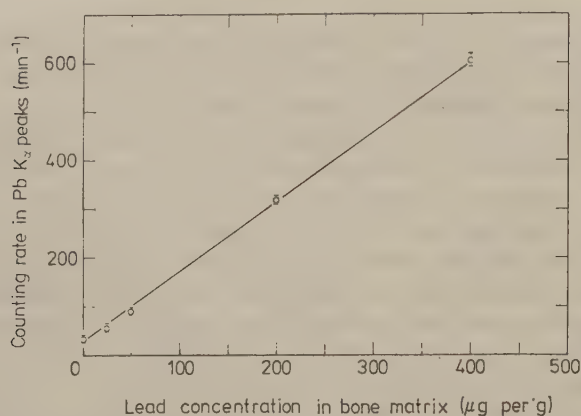


Fig. 3. Counting rate in Pb K_{α} peaks for finger phantoms with different lead concentrations in the bone simulating part.

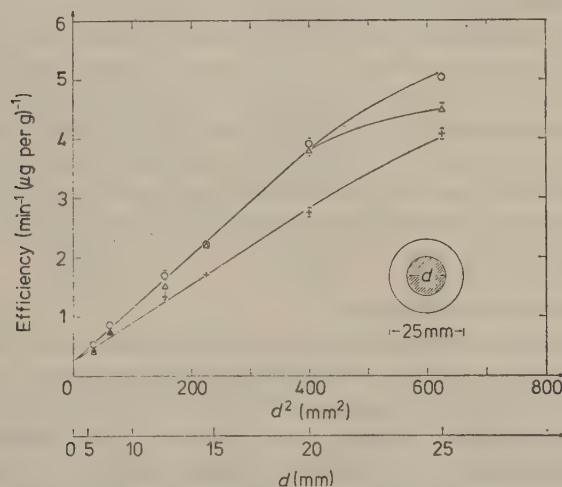


Fig. 4. The efficiency for lead detection in finger phantoms with 30% (Δ), 20% ($\circ$) and 10% (+) bone mineral in bone cylinders of diameter d . The lead concentration in the bone-simulating part is $200 \mu\text{g per g}$.

importance ($1\text{--}2 \mu\text{g Pb per g}$) as shown by atomic absorption spectrophotometry.

The counting rate in the lead K_{α} peak is also dependent on the bone volume which is examined. This is seen in fig. 4 which shows the linear relation between the counting rate per unit lead concentration and the volume ($\propto d^3$) of the bone cylinder up to 20 mm diameter. For larger diameters some part of the bone cylinder will not be seen by both the detector and the radiation source. Therefore, the efficiency for lead detection no longer exhibits a linear relation with respect to the volume of the bone cylinder.

A higher bone mineral concentration in the bone cylinder (which consists of silica paraffin wax and bone ash) implies increased density. Therefore, bone cylinders with equal lead concentration will contain more lead when the bone mineral concentration increases. This is indicated in fig. 4 where the counting rate from bone cylinders with 10% bone mineral concentration is lower than that for the 20% and 30% bone mineral phantoms. The increasing density and atomic number of the bone cylinders will also result in a higher attenuation of the 122 keV photons and the lead K_{α} X-rays. This explains why the curves from the 20% and 30% bone mineral phantoms coincide.

To estimate the bone mineral concentration in the examined volume the quotient of the observed counting rate of the 90° coherent scattered 122 keV photons and the 90° Compton scattered 122 and 136 keV photons is calculated in fig. 5. The quotient varies slowly with the bone mineral concentration

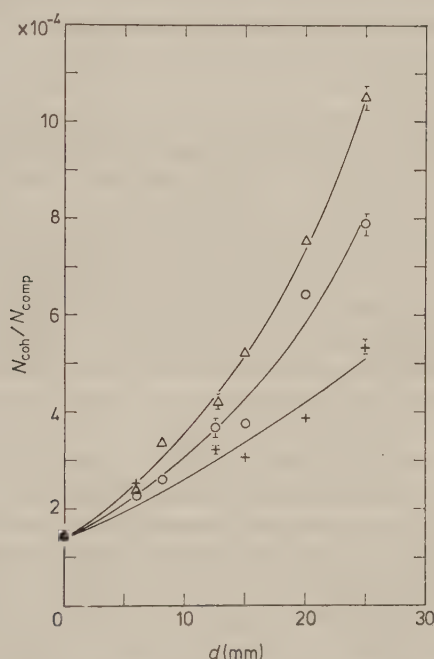


Fig. 5. The ratio ($N_{\text{coh}}/N_{\text{comp}}$) between the number of 90° coherent scattered 122 keV photons and 90° Compton scattered 122 and 136 keV photons for different bone diameters d , measured with 30% (Δ), 20% ($\circ$) and 10% (+) bone mineral in the bone cylinder.

in the volume examined since the major part of this volume contains soft tissue phantom material. As seen from fig. 4 the uncertainty in the observed lead concentration of a finger with a well known bone diameter in the interval between 10 and 15 mm is 25–30% due to the unknown bone mineral concentration in the finger. The method is more dependent on the measuring geometry than on the bone mineral concentration because of the small distances between the radiation source, sample and detector. For known bone

mineral concentration an increase in diameter from 10 to 15 mm increases the lead K_{α} counting rate by 90%. A more collimated detector-source geometry is less sensitive to variations of the bone diameter but would have a higher detection limit.

4. Calibration of *in vivo* measurements

The calibration technique was used to estimate the lead concentration in the skeleton of a man with a high ($0.70 \mu\text{g per g}$) lead concentration in the blood. Measurements were carried out on his left and right forefinger, on the right little finger and on the tibia. The fingers were carefully washed before the measurements to exclude external contamination. A statistically significant net number of pulses was recorded in the lead $K_{\alpha 1}$ and $K_{\alpha 2}$ regions of the pulse height distribution from all measuring sites. The lead concentration in the skeleton was estimated from the finger measurements. The lead concentration in the tibia was of the same order as the lead concentration in the fingers and this confirmed the absence of any significant external contamination on the fingers.

The diameter of the finger bones was estimated from an X-ray study. The bone mineral concentration was estimated from the quotient of the number of coherent scattered 122 keV photons and Compton scattered 122 and 136 keV photons and was found to correspond to the 10% bone mineral phantom. The lead concentration in the finger bones was determined as $74 \pm 11 \mu\text{g per g}$ (mean value $\pm$ SE) from measurements on finger phantoms with identical size and bone mineral concentration to the real finger. The distribution of lead within the finger bones of our patients is not known. However, the registration efficiency within a typical finger bone varies only $\pm 20\%$ at the most (compare fig. 2), which means that a phantom with homogeneously distributed lead could be used.

The finger phantoms were also used to verify the earlier estimated lead concentrations in the skeletons of five retired workers from a metal industry. This new calibration technique yields approximately the same lead concentration; that is, $50 \pm 5 \mu\text{g per g}$ in the forefingers compared with $55 \pm 8 \mu\text{g per g}$ from the earlier method where the finger measurements were calibrated by perspex tubes filled with lead solution (Ahlgren *et al.* 1976). The detection limit corresponding to three standard deviations above the background achieved with a 740 MBq (20 mCi) ^{57}Co source, a 15 min measuring time on a forefinger phantom with a 12.5 mm bone diameter is $14 \mu\text{g per g}$.

5. Summary and conclusion

The following steps can be recommended for a finger measurement.

Geometry. The diameter of the bone in the finger is measured from two orthogonal X-ray projections. The exact diameter of the bone is important in the calibration and should be measured with an accuracy of $\pm 1 \text{ mm}$.

Bone mineral concentration. The bone mineral concentration is estimated from the quotient of the coherent and Compton scattered primary photons. As seen

from fig. 4 this value is not critical for the calibration, particularly as a bone mineral concentration of 30% or more seldom occurs in a human finger (ICRP 1975).

The lead concentration in the finger bone is then derived from a measurement on a finger phantom made of silica paraffin wax and bone ash with the same size and bone mineral concentration as the real bone.

Professor Kurt Lidén has contributed to this work with valuable suggestions and constructive criticism. This investigation was supported by grants from the Swedish Work Environment Fund.

RÉSUMÉ

Une technique de fluorescence aux rayons X pour la détermination *in vivo* de la concentration de plomb dans la substance intercellulaire d'un os

Nous avons déjà décrit le dépistage *in vivo* du plomb dans le squelette d'un homme au moyen d'une analyse de fluorescence aux rayons X, en se servant d'une source de 740 MBq ^{57}Co pour l'excitation et d'un détecteur d'1 cm³ Ge(Li) pour l'enregistrement du rayonnement Pb K_α et K_β. Les variétés de géométrie, de densité et de composition atomique des tissus intéressants (surtout les doigts) soulèvent certains problèmes lorsqu'il s'agit d'évaluer la concentration réelle d'un élément donné. Un fantôme de doigt cylindrique à deux éléments fut donc construit à partir de paraffine au silicium et de cendre d'os d'animaux. Le diamètre de l'os du doigt a été évalué au moyen de radioscopie dans deux projections orthogonales. La concentration minérale de l'os a alors été évaluée d'après le quotient du nombre de photons primaires cohérents et à diffusion Compton. La concentration de plomb dans les os du doigt fut tirée d'une mesure du fantôme de doigt fait au moyen de paraffine au silicium et de cendre d'os, ayant la même dimension et la même concentration minérale dans l'os que l'os réel. La concentration minimum dépistable de plomb dans un os de doigt était de 14 µg g⁻¹ pour 15 min de temps de mesure. La concentration de plomb mesurée chez des ouvriers d'une industrie du métal était de l'ordre de 40 à 100 µg g⁻¹.

ZUSAMMENFASSUNG

Eine Röntgen-Fluoreszenz-Methode zur *in vivo* Bestimmung von Bleikonzentrationen in einer Knochengrundsubstanz

Zu einem früheren Zeitpunkt haben wir über die Feststellung von Blei im menschlichen Skelett mittels der Röntgen-Fluoreszenz-Analyse berichtet, wobei eine 740 MBq ^{57}Co -Quelle zur Erregung und ein 1 cm³ Ge(Li) Detektor zur Registrierung der Pb K_α und K_β Strahlung verwendet werden. Die unterschiedliche Geometrie, Dichte und atomare Zusammensetzung der Gewebe von Interesse (in erster Linie die Finger) werfen eine Reihe von Problemen bei der Beurteilung der genauen Zusammensetzung eines gegebenen Elementes auf. Deshalb wurde ein zylindrisches Fingermodell aus Siliziumdioxid-Paraffin-Wachs und tierischer Knochenasche konstruiert. Der Durchmesser des Fingerknochens wurde aufgrund von Röntgenuntersuchungen in zwei orthogonalen Projektionen berechnet. Die Knochenmineralkonzentration wurde dann mit Hilfe des Quotienten aus der Anzahl der kohärenten und Comptongestreuten Primärphotone berechnet. Die Bleikonzentration in den Fingerknochen wurde dann durch Messungen bei einem Fingermodell aus Silizium-Dioxyd-Paraffinwachs und Knochenasche mit der gleichen Grösse und Knochenmineralkonzentration wie der echte Knochen ermittelt. Die niedrigste feststellbare Bleikonzentration in einem Fingerknochen betrug 14 µg g⁻¹ bei einer Messzeit von 15 min. Die bei Arbeitern in der Metallindustrie gemessenen Bleikonzentrationen lagen im Bereich zwischen 40–100 µg g⁻¹.

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IN VIVO DETERMINATION OF LEAD IN THE SKELETON FOLLOWING OCCUPATIONAL EXPOSURE

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ABSTRACT

The concentrations of lead in the fingerbones of 22 subjects earlier occupationally exposed in a storage battery plant have been compared with values of the lead concentration in their blood, 7 years having elapsed since the end of the exposure. The lead concentration in bone was measured in vivo using an X-ray fluorescence technique in which two ⁵⁷Co γ-ray sources were used for generating the characteristic X-rays of lead and a Ge(Li) detector for measuring them. For three subjects, the variation of the lead concentration along the forefinger was also measured as well as the lead concentration in the tibia. The measured lead concentration in the fingerbones were between 20 μg·g⁻¹ (our detection limit) and 118 μg·g⁻¹. The lead concentration in the fingerbone was found to increase with the period time of employment, but no simple relation between the lead concentrations in the blood and in the forefinger bone was found.

The decrease in the lead concentration in the blood after the end of the exposure was followed in 4 subjects. Seven years after the end of exposure, the lead concentration in the blood was found to be more dependent on the daily intake of lead than on the release of lead from the skeleton. These experimental results could be explained by a two-compartment model using exchangerates given in the literature. This model has also been used to calculate the lead concentration in the blood which could be reached following a sudden release of lead from the skeleton.

1 INTRODUCTION

The skeleton contains about 90-95% of the total body burden of lead (Barry and Mossman, 1970; Schroeder and Tipton, 1968). Measurements of lead concentration in the skeleton are therefore of fundamental importance for estimating the total body burden of lead. In earlier publications (Ahlgren et al, 1976; Ahlgren et al, 1977; Ahlgren and Mattsson, 1979), we have reported *in vivo* detection of lead in the skeleton of lead workers using X-ray fluorescence analysis. This paper deals with a comparison between the lead concentrations in the blood and in the skeleton as determined in fingerbone by X-ray fluorescence analysis *in vivo*. The determinations were carried out on subjects whose occupational exposure to lead terminated seven years prior to the study.

2 MATERIALS AND METHODS

Twenty-two men, aged 27-75 ($\bar{x}=57$) years, who had earlier worked in a storage battery plant for periods from 0.8 and 45 ($\bar{x}=22$) years were studied. At the time of the measurements, the factory had been closed for 7 years and since that time none of the subjects studied had been occupationally exposed to lead. Blood samples for determination of the lead content were collected at the time of the *in vivo* measurement and analysed by atomic absorption spectrophotometry (Schütz and Skerfving, 1976). For some of the persons studied, the variation of the lead concentration in the blood was also followed during the first year after the closing-down of the factory. In our determination of lead in the skeleton, the lowest detection limit (20 $\mu\text{g Pb}$ per gram fresh weight) is reached when the measurements are carried out on the fingers. The lead concentration in the 2nd phalanx of the left forefinger was therefore determined for all the participants in this study. The fingers were carefully washed with water and detergent before the measurements in order to remove possible skin contamination with lead. For three of the subjects, measurements were also carried out on the proximal and distal joints of the left forefinger as well as on the upper part of the tibia (table 1). In normal measurements, a small volume (about 1 cm^3) of the 2nd phalanx of the bone of the left forefinger was irradiated for 40 minutes with two collimated ^{57}Co sources (0.6 and 0.2 GBq) as shown in fig 1. The count rates of characteristic X-rays emitted from lead in the irradiated bone volume were measured with a Ge(Li) spectrometer (16 mm diameter x 5.2 mm; energy resolution: FWHM=750 eV at 75 keV). The angle between the incident and measured radiation was around 90°. The collimator in front of the detector and the radiation shield was made of high purity tin partly covered with gold (fig 1). The mean diameter of the bone measured was calculated from two X-ray pictures taken in orthogonal projections. To relate the count rates of characteristic lead X-rays to lead concentration in the bones of the finger, measurements on finger-like phantoms with known concentrations of lead in their bony part and with various bone dimensions were carried out as described by Ahlgren and Mattsson (1979).

Radiation dosimetry: The absorbed dose rate to the finger was measured with small (2x2x1 mm^3) extruded LiF dosimeters. The absorbed dose at the surface of the skin was 5.5 mGy (550 mrad) and to the centre of the finger it was 2.5 mGy (250 mrad) per 40 minutes. Since the total volume of the finger (bone and soft tissue) irradiated always was less than 3.5 cm^3 , the total absorbed energy was much smaller than in an ordinary X-ray examination of the hand. (See table 2).

3 RESULTS AND DISCUSSION

A fundamental question is how well the lead concentration in the bone of the forefinger represents the mean lead concentration in the skeleton and thus the total body burden of lead. Table 1 shows the results of measurements of the lead concentration in different parts of the skeletons of 3 highly contaminated persons. The concentrations in three different regions of the left forefinger are not significantly different. A significant difference between the lead concentration in forefinger bone and in the tibia could only be detected for one person (SL) (see table 1). It must, however, be pointed out that the uncertainty in the tibia measurements was considerably larger than in the finger measurements. This means that concentration differences between fingerbone and tibia of up to 50% could be present without their being registered as significantly different.

Of the 22 men studied, 15 (70%) had lead concentrations in fingerbone larger than $20 \mu\text{g}\cdot\text{g}^{-1}$, which was the limit of detection. The lead concentration in fingerbone was found to increase with the period of employment as can be seen in figure 2. The variation of the lead exposure with time and from worker to worker is only very poorly known. However, increased health care certainly lowered the lead exposure during the last years of the exposure period. The shortest period of exposure giving a measurable lead concentration in the fingerbones was 3 years. Figure 3 shows the lead concentrations in the skeleton and the blood for 15 workers, the periods of employment being roughly indicated in the figure. The mean value for lead concentration in the blood for males from the same part of Sweden but with no known occupational exposure to lead is $0.4 \mu\text{mol}\cdot\text{l}^{-1}$ (range $0.2\text{--}0.9 \mu\text{mol}\cdot\text{l}^{-1}$)^x (Haeger-Aronsen and Schütz, 1968). From lead concentrations in the skeleton derived from autopsy samples taken from 126 non-occupationally exposed Danes, the total body burden of lead has been estimated to be 22 mg (Grandjean, 1973). A point (⊕) representing the mean values mentioned above are also shown in figure 3. Assuming that the lead concentration in the finger bone reflects the body burden, figure 3 indicates that even 7 years after the end of exposure to lead there exists no simple relation between the total body burden of lead and the lead concentration in the blood.

Three subjects A, B and C deviate from the rest of the group by having ratios between the lead concentrations in the skeleton and in the blood which are 2-3 times larger than for the other persons. The subject marked A was exposed to lead oxide dust for 43 years. B was highly exposed to lead oxide dust during the first 20 years of employment. During this period, he several times showed acute symptoms of lead poisoning. During the last 20 years of employment, his lead exposure was very low. Subject C was exposed for 35 years, but the degree of his exposure cannot be reliably estimated. The person marked D in figure 3 worked for 45 years mainly with the melting of metallic lead. Figure 4 shows the variation of the lead concentration in the blood for persons A, B, C and D after exposure. The rapid decrease in the lead concentration in the blood after exposure may represent the washout of lead from the soft tissue pools. The figures suggest that 7 years after the end of exposure, lead concentration in the blood of these highly contaminated persons were more dependent on their normal daily intake of lead than on the total body burdens. This result can also be predicted using a two-compartment model describing the kinetics of lead in the body as shown in figure 5. Compartment 1 represents the blood, liver and muscles and compartment 2 the skeleton. The exchange rates λ_{12} (from compart-

^x) $1 \mu\text{mol}\cdot\text{l}^{-1} = 20.83 \mu\text{g}/100 \text{ ml}$

ment 1 to 2) and λ_{10} have been calculated assuming the steady state condition described by the ICRP (1975) with 110 mg lead in the skeleton, 6.2 mg lead in the blood, liver and muscles (of which 1.40 mg is in the blood) and a daily absorption of 40 μg . Two different exchange rates (λ_{21}) from the skeleton to the blood have been used, one being taken as the mean skeletal turnover rate of 3.5% a year (Rivera, 1965) and the other as the turnover rate for femur-like bones, 1.5% a year (Rivera, 1965).

By using these calculated exchange rates and a daily absorption of 15 μg , the lead concentration in the blood will after 55 years reach a value of $0.43 \mu\text{mol}\cdot\text{l}^{-1}$ ($0.09 \mu\text{g}\cdot\text{g}^{-1}$) and that in the skeleton will be between 2 and $3 \mu\text{g}\cdot\text{g}^{-1}$ as seen in figure 6. These values are in good agreement with the corresponding values for non occupationally exposed subjects in Sweden. These results further indicate the validity of the calculated exchange rates. The same kinetic model has been used to predict the decrease in the lead concentration in the blood after the end of a long occupational exposure. For this calculation, the lead concentration at the end of the exposure was taken to be $80 \mu\text{g}\cdot\text{g}^{-1}$ in the skeleton and $3.4 \mu\text{mol}\cdot\text{l}^{-1}$ ($0.7 \mu\text{g}\cdot\text{g}^{-1}$) in the blood. These values are typical for the most exposed subjects in our study. Our kinetic model predicts that 7 years after the end of the exposure the lead concentration in the skeleton will be $68\text{--}74 \mu\text{g}\cdot\text{g}^{-1}$ and in the blood between 1.9 and $1.2 \mu\text{mol}\cdot\text{l}^{-1}$ assuming transfer rates of lead from the skeleton to the blood of 3.5% and 1.5% per year respectively.

Figure 6 also shows a point ($\square$) representing the mean value for the measured blood concentration for 5 persons having about $70 \mu\text{g}\cdot\text{g}^{-1}$ in the skeleton 7 years after the exposure. The lead concentration in the blood which originates from the skeletal pool is very dependent on the exchange rate from the skeleton. The low concentrations in the blood of these formerly occupationally exposed persons indicates an exchange rate from the skeleton of 1-2% a year. This low value rate can be explained by the fact most of the lead in the skeleton of the persons was acquired during the first part of their 30 year exposure when lead exposure in the factory was very intense. The lead in the more easily exchangeable parts of the skeleton may therefore already have been released.

The large amount of lead stored in the skeletons of these persons represents a potential risk should it be suddenly released. In table 3 we have calculated the lead concentration in the blood after a release of 1 to 10% of the lead in the skeleton during 1, 5 or 12 months. The calculations have been carried out using the kinetic model in figure 5 with $\lambda_{12} = 0$ and with λ_{21} and λ_{10} as given in table 3. The calculated blood level after a sudden release is high in comparison with the limit value for occupational exposure, $3.4 \mu\text{mol}\cdot\text{l}^{-1}$ ($0.7 \mu\text{g}\cdot\text{g}^{-1}$). These values are theoretical calculations and may represent an upper limit for lead concentration in blood. The exponential increase in lead excretion in urine with increasing concentration of lead in the blood noted by Schütz and Skerfving (1976) indicates that the excretion rate λ_{10} increases with increasing blood lead concentration, thus lowering the real blood lead concentration.

4 SUMMARY

The lead concentration in the skeleton of 22 occupationally exposed men as determined *in vivo* on forefinger bone have been compared with the lead concentration in their blood 7 years after the end of their exposure to lead. For three persons, the concentration of lead along the finger and in the tibia was also studied.

No statistically significant variation of the concentration along the forefinger bone could be detected.

15 of the 22 men had a lead concentration in the forefinger bone exceeding the detection limit of $20 \mu\text{g}\cdot\text{g}^{-1}$, the concentration being found to increase with the period of employment. No simple relation between the concentrations in the blood and skeleton could be found.

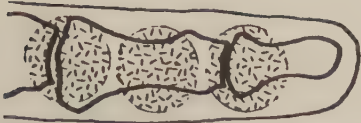
A two-compartment model describing the kinetics of lead in the body has been used to verify the measured lead concentration in blood and skeleton several years after the end of an occupational exposure.

The results of this work indicate the necessity of carrying out measurements on the skeleton of living man to have a proper estimate of the total body burden of lead and hence information on the potential risk associated with a certain lead contamination.

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erythrocyte δ -aminolevulinic acid dehydratase activity and urinary
excretion of lead, δ -aminolevulinic acid and coproporphyrin.
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Person	Tibia			
SL	117±9	118±12	135±12	62±19
P0	59±7	65±10	89±9	85±18
HB	81±10	94±13	85±11	84±21

Table 1. Lead concentration ($\mu\text{g}\cdot\text{g}^{-1}\pm 1\text{ SD}$) in the forefinger bone and in the tibia.

Type of investigation	Mean absorbed dose mGy	Absorbed energy mJ
X-ray fluorescence analysis of finger	2.5	10^{-2}
X-ray examination of hand	0.65	$(10-25)\cdot 10^{-2}$

Table 2. Mean absorbed dose and absorbed energy

Percent of total lead which is released	Period during which the lead is released d	Excretion rate, $\frac{\lambda_{21}}{\text{d}^{-1}}$	Maximal calculated lead concentration in blood $\mu\text{mol}\cdot\text{l}^{-1}$
1	30	0.330 ± 10^{-3}	2.5
5	30	0.167 ± 10^{-2}	7.3
10	30	0.330 ± 10^{-2}	12.8
10	180	0.556 ± 10^{-3}	8.2
10	360	0.278 ± 10^{-3}	5.4

Table 3. The calculated lead concentrations in the blood after release of part of the total skeletal lead. The calculations have been carried out for a person with an initial lead concentration of $70\mu\text{g}\cdot\text{g}^{-1}$ in the skeleton and $1.4\mu\text{mol}\cdot\text{l}^{-1}$ in the blood and with an excretion rate λ_{10} of $0.650\cdot 10^{-2}\text{ d}^{-1}$.

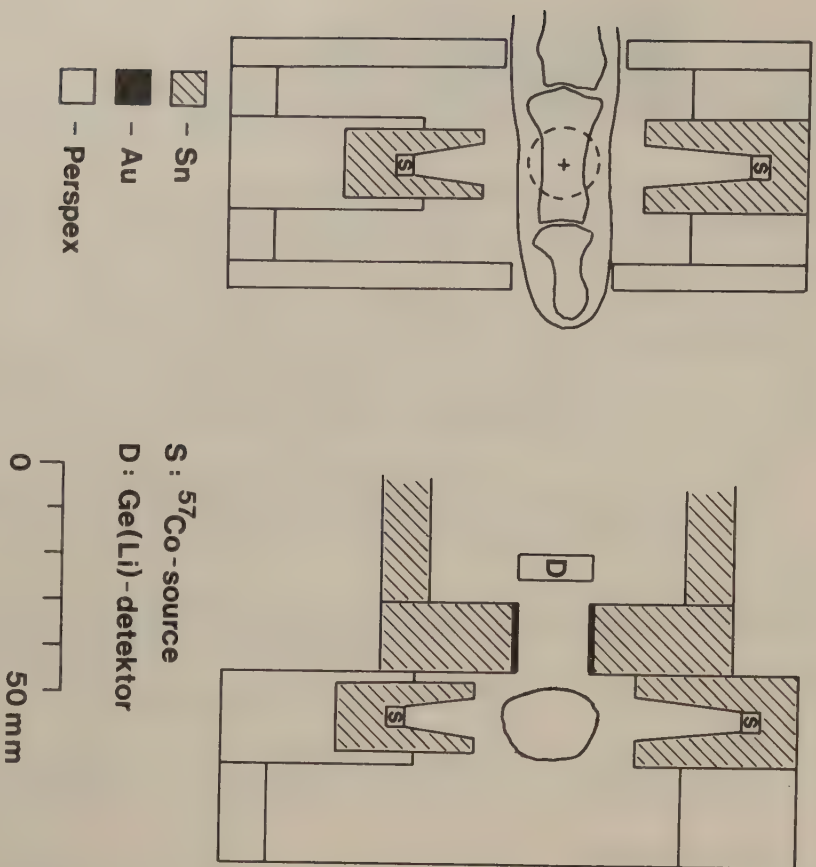


Figure 1 The arrangement for the determination of lead in the forefinger bone by X-ray fluorescence analysis. The radiation shield, the two ^{57}Co sources, the detector collimator with its gold covered opening and the perspex holder for the finger are shown.

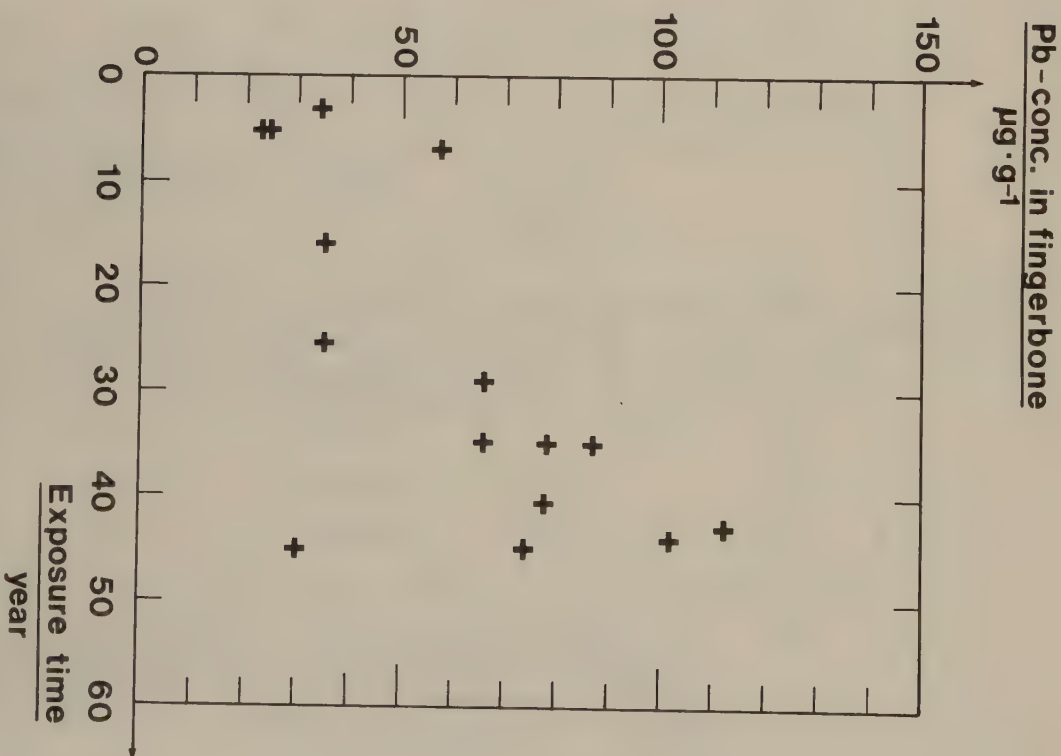


Figure 2 The measured lead concentration in the forefinger bone of persons with different periods of occupational exposure.

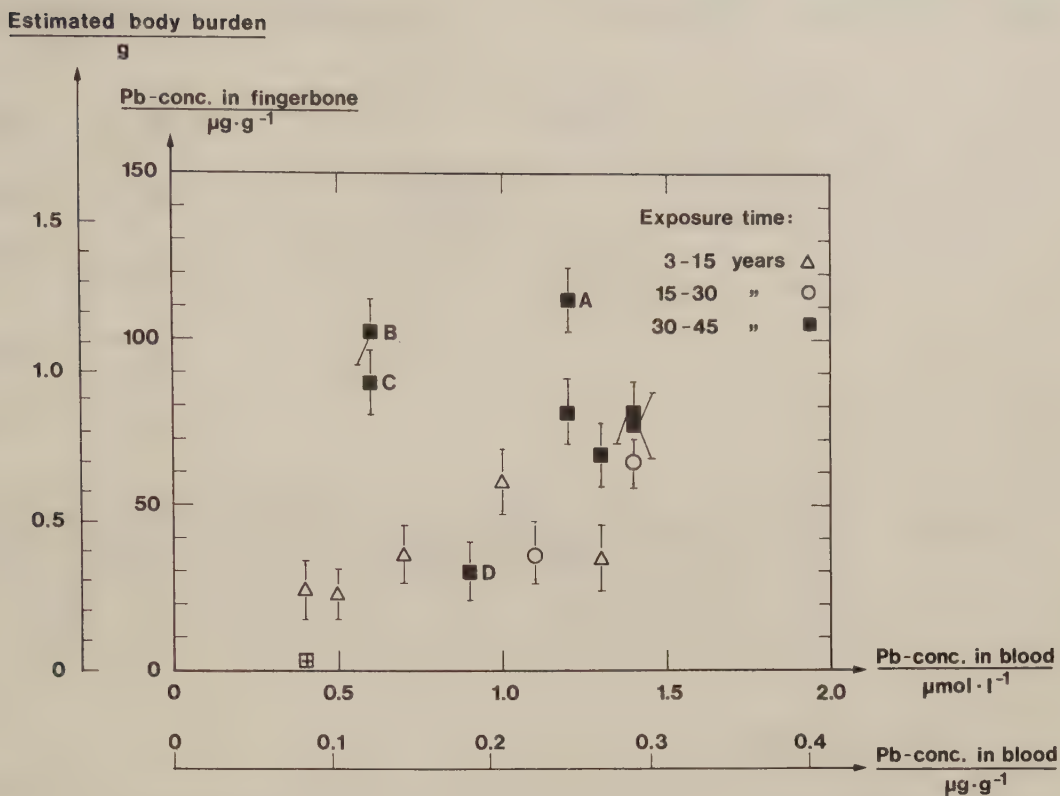


Figure 3 The measured lead concentrations in forefinger bone and blood for occupationally exposed persons. The total body burden of lead is estimated assuming that the lead concentration in the forefinger bone represents the lead concentration in the whole skeleton. A point ($\boxtimes$) representing these values for non occupationally exposed persons is also given. The indicated uncertainty is due to counting statistics.

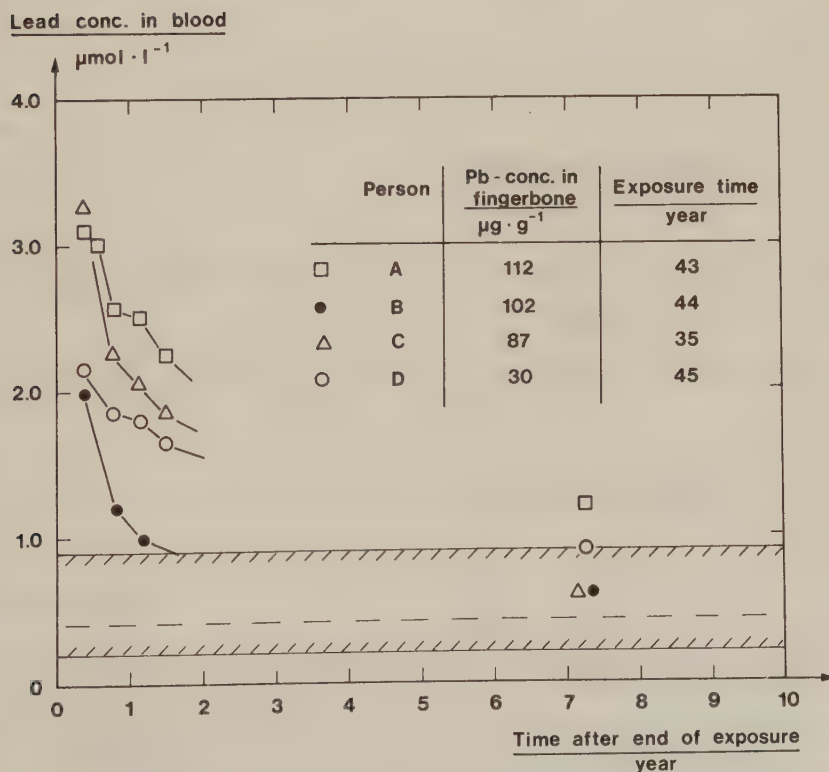


Figure 4 The measured lead concentrations in the blood at different times after the end of the occupational exposure. The mean value and the range of the lead concentration in blood for non occupationally exposed persons is indicated.

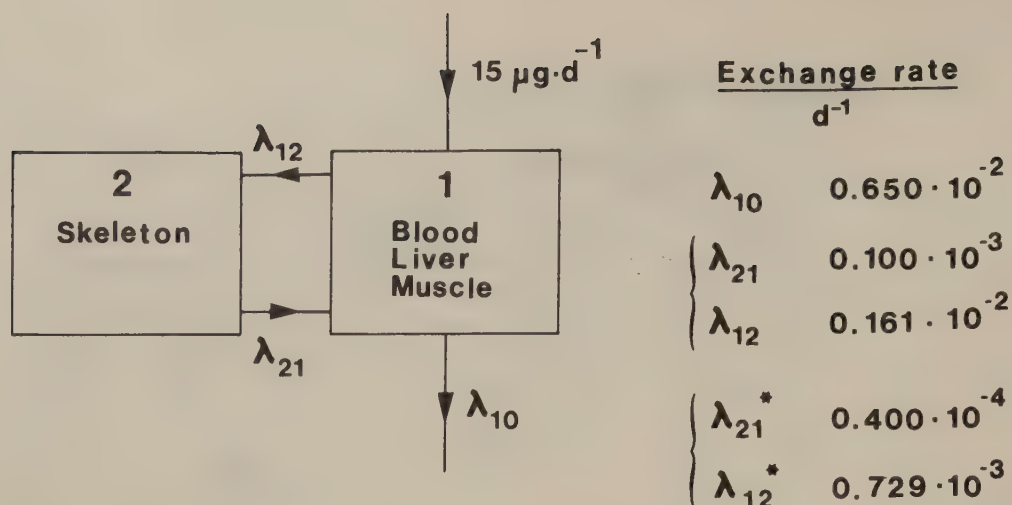


Figure 5 The two-compartment model which was used to describe the kinetics of lead transfer between skeleton and blood. The two different exchange rates λ_{21} and λ_{21}^* for the transfer of lead from the skeleton to the soft tissue pool correspond to annual turnover rates for the skeleton of $3.5\% \cdot a^{-1}$ and $1.5\% \cdot a^{-1}$ respectively.

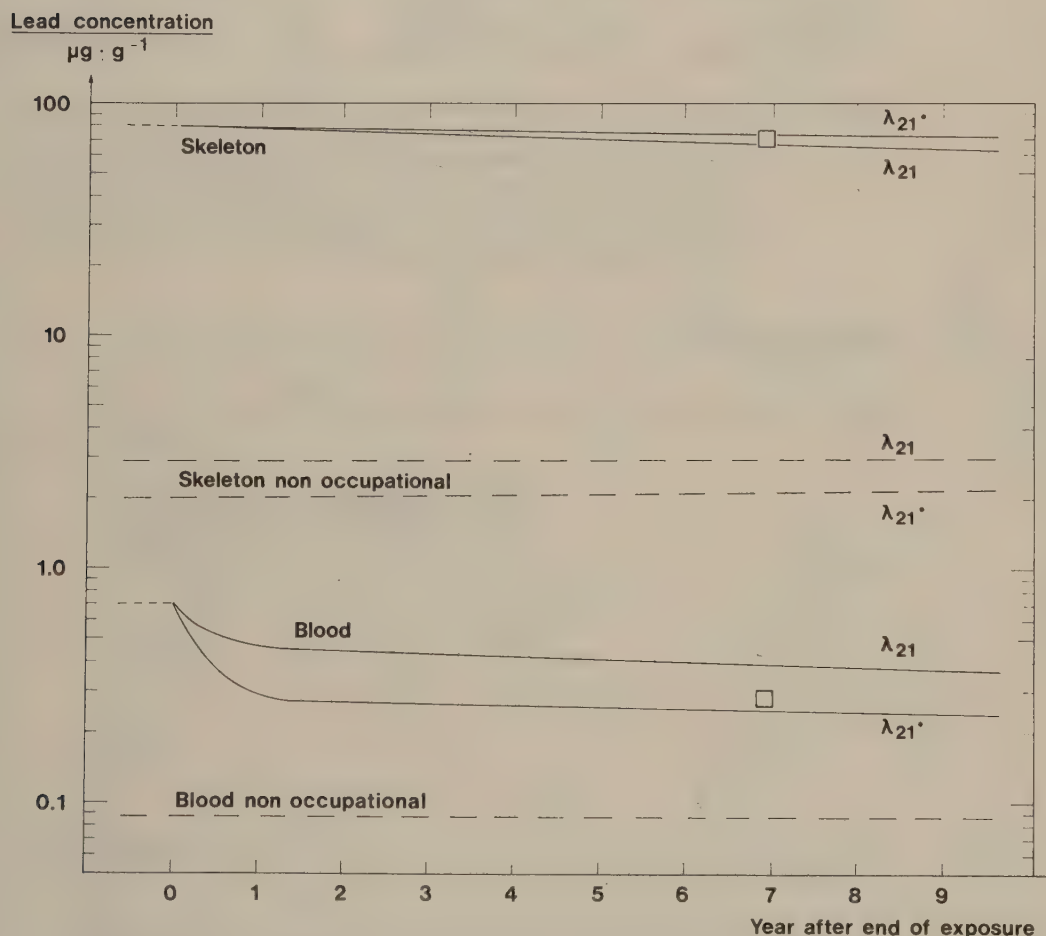


Figure 6 Lead concentrations in the skeleton and blood at different times after the end of occupational exposure as calculated from the two-compartment model. A point (□) represents the mean value of the measured blood concentration of 5 persons having about $70 \mu\text{g} \cdot \text{g}^{-1}$ in their skeletons 7 years after the exposure. The calculated lead concentrations in the skeleton and blood for non occupationally exposed persons are also given.

DISTRIBUTION OF LEAD IN ARCHAEOLOGICAL ROMAN SKELETONS MEASURED
BY NON DESTRUCTIVE X-RAY FLUORESCENCE ANALYSIS

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The lead concentration in bones from archaeological Roman skeletons has been measured by non-destructive X-ray fluorescence analysis using the ratio between the number of Pb K X-rays and primary photons incoherently scattered at 90° . The bone mineral concentration was estimated from the ratio between the coherently and incoherently scattered photons. From these results, lead concentration in fresh bone could be reconstructed using data from the literature for the ratio between mineral weight and fresh weight for various bones. The results from four skeletons show variations in lead concentration by a factor of four (based on fresh weight) between various bones in the skeleton. The results indicates that the average skeletal concentration may be estimated within 50% from a single measurement of the finger phalanx.

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INTRODUCTION

In estimating the total body-burden of lead from single in vivo measurements on finger bones by means of X-ray fluorescence analysis (1, 2) it is important to know both how lead is distributed in the skeleton and the concentration-gradient in the single bone on which the measurement is made. The sensitivity of the X-ray fluorescence technique is not high enough to permit detailed studies of the distributions in living persons even if they have been occupationally exposed to lead. Such studies might, however, be possible on autopsy material using atomic absorption spectrophotometry. Another possibility is to use archaeological samples from periods when the intake of lead was much higher than today. In such samples, the lead concentration may be so high that X-ray fluorescence analysis can be used. The purpose of this work was to study the distribution of lead in archaeological Roman skeletons by means of non-destructive X-ray fluorescence analysis.

MATERIAL

The lead concentrations in various parts of four human skeletons from the Roman British cemetery at Cirencester in England have been studied. This cemetery dates back to the third and fourth centuries A.D. Samples of rib, skull, fibula, phalanx and metacarpal or metatarsal bone have been studied. The phalanx and the metacarpal or metatarsal bones have been chosen since they represent the same bone or the same types of bone as used for our in vivo studies (2). Fibula was chosen to represent the long compact bones and the skull and the rib samples represent the spongier bone of the skeleton.

METHODS

The quotient between the count rate of the characteristic X-rays of lead and that of those primary photons incoherently scattered in the sample towards the detector has been used to calculate the lead concentration in the bone samples. The cross-section for incoherent scattering is proportional to the electron density. Since the number of electrons per unit mass is almost constant for most of the elements contained in biological matrices, the count rate of incoherently scattered photons is proportional to the mass of the irradiated sample which is seen by the de-

tector. Hydrogen is unique in that it contains about twice as many electrons per unit mass as other elements and hence has about twice the average cross-section. However, hydrogen is a light element and therefore gives only a small contribution to the total mass. When incoherent scattering is the dominant interaction mode for the incident photons as well as for characteristic X-rays, the quotient between the characteristic X-rays and the incoherently scattered photons will be approximately independent of the density and of the atomic composition of the matrix and hence proportional to the concentration of the trace element.

Water, sawdust and bone ash containing known amounts of lead ($100 - 10000 \mu\text{g} \cdot \text{g}^{-1}$) were used to simulate various biological matrices. Measurements on various amounts of these matrices were carried out to study if the quotient is independent of the mass investigated.

The lead concentration in the Roman bone samples was measured at different positions along the bones as shown in figure 3. The quotient of the coherently and incoherently scattered photons from the bone measurements was compared with that of measurements of bone ash to see how much of the bone samples consisted of inorganic material. At the time of the measurements the bone samples were dry and the soil had been removed from them. No other sample preparation was carried out.

The experimental set-up has been described elsewhere (2). The lead-containing sawdust, bone ash and water were measured in 5 ml plastic containers with thin walls which were outside the investigated volume as seen in figure 1.

RESULTS AND DISCUSSION

Measuring technique

Figure 1 shows that the count rate of incoherently scattered photons is proportional to the mass of water in the container even when only small amounts of water at the foot of the container are present. Figure 2 shows that the quotient between the count rate of the characteristic K_{α} X-rays of lead and incoherently scattered photons is independent of the density and of the atomic composition of the surrounding matrix. These results have been shown to be valid for concentrations between $100 - 10000 \mu\text{g} \cdot \text{g}^{-1}$. This means that the count rate of the characteristic X-rays of lead from bone samples of various shapes and densities can be correlated to the true lead concentration in the bone sample by mea-

surements on lead solutions of known concentrations. Measured lead concentrations will represent mean values of the bone volumes investigated.

The calibration technique described is very suitable for determining trace element concentrations in various other samples, e.g., hair, fingernails, solutions and dust since such samples can be measured directly without extensive sample preparation.

Lead distribution in Roman skeletons

It is known that the Romans used kitchen utensils made of lead and lead pipes for drinking water. The most important source of lead intake for people of the upper social classes was a special wine-additive called sapa which was used to sweeten and preserve it. This was prepared by evaporating grape juice to one third of its original volume in a leaden pot. The lead had two virtues, only one of which was understood correctly that it gave a slightly sweetish taste. However more important was the fact that it poisoned the microorganisms causing fermentation and souring (4).

In all the bones from the four graves studied, lead concentrations between 80 and 1000 $\mu\text{g} \cdot \text{g}^{-1}$ were found. Table 1 shows the lead concentration in the different bones studied. Figure 3 shows the distribution of lead in fibula, metacarpal, phalanx and in samples of skulls and ribs from grave No 14. In figure 4, the lead distribution along the phalanx and the metacarpal bone from the same grave has been studied in detail. These bones were selected for detailed study because they were very well preserved.

To be able to compare the lead concentrations measured in the archaeological samples with those from our in vivo measurements, it is important to know the ratio between the weights of fresh bone and the weight at the time of measurement. As seen from the quotient of coherently and incoherently scattered photons in figure 5, the bones consist of approximately 80% inorganic material. This quotient was almost constant for the different bones in the skeleton and along the long bones. Using the ratio between ash weight and fresh weight for compact and spongy bone given by Strehlow and Kneip (5) and by the ICRP (6), the ratios between the actual weight of untreated bone and fresh weight of these bones were taken as 0.50 for compact bone and 0.25 for spongy bone. The calculated lead concentration per mass unit of wet weight will be very dependent on the actual value of this ratio used. Obviously, a sharp boundary cannot be drawn between

the two types of bone as they are merely different arrangements of the same histological elements.

As seen in table 1 and figure 3 and 4, the measured concentrations of lead at the ends of fibula and the fingerbones are up to three times as high as in the shaft.

When the lead concentration in the bone samples is estimated in terms of the fresh weight, the lead concentration at the ends will be even lower than in the shaft (see table 1). This is in agreement with Strehlow and Kneip (5) who found 39% lower lead concentration per fresh weight unit in the end than in the shaft.

In our earlier in vivo measurements, no significant variation with position was found in measurements along the forefinger of three retired persons who had been exposed to lead. (2).

Due to the large uncertainties in the above estimates the results of the present work are not inconsistent with the results of our earlier in vivo measurements.

The average concentrations per fresh weight in the skeleton from the four graves have been calculated assuming that the skeleton is composed by 45% fibula-like bones, 25% rib-like bones and 10% metacarpal-like bones and that 25% of the bones are similar to the skull. The composition of fibula-like bones has been taken to be 75% shaft and 25% end bones and that of the metacarpals as 50% shaft and 50% end bones. These values are estimates based on data given by the ICRP (6). As seen from Table 1, it appears as if the lead concentration per fresh weight of the finger phalanx is higher than the estimated average skeletal concentration based on measurements on several representative bones from the skeleton. The actual weight to fresh weight ratio of the phalanx has been taken as 0.50, the value used for fibula and other long bones. As seen from figure 4, this may be an overestimate, since measurements of the shafts of such short bones will include approximately 50% end bones and 50% shaft bones. Using a weight/fresh weight ratio between 0.50 and 0.25 would give better agreement with the average skeletal concentration. Taking this into consideration, the total body-burden may be estimated to within 50% from a single measurement of the finger phalanx.

The total amount of lead in the skeleton of the most exposed subject in table 1 is approximately 1.5 g. The daily intake of lead during a 25-year period from food has been estimated to be 12 mg, assuming a constant rate of intake and single exponential elimination. The half-life of lead in the skeleton has been taken as 20 years (7) and the fraction of the

ingested lead reaching the skeleton as 2% (8). This calculated daily intake of 12 mg should be compared with 0.1 - 0.2 mg for non-occupationally exposed persons in England today (9). If wine was the major source of lead intake for Romans, an average concentration of $60 \mu\text{g} \cdot \text{g}^{-1}$ and a daily consumption of 20 cl wine would be required to reach this body-burden. The skeletons were recovered between 1970 - 74 and the sites was covered with uniform black soil to a depth of 1.2 - 1.4 metres above the layer of natural limestone. The soil lead concentration at the findings was $14 \mu\text{g} \cdot \text{g}^{-1}$ (dry weight). The large difference in lead concentration between bones and soil indicates that the exchange of lead from the bones is very slow. This has also been suggested by Grandjean (10).

Barium was also detected in all the bones its concentration being approximately 30 - 40 $\mu\text{g} \cdot \text{g}^{-1}$ (archaeological weight). This value is in agreement with that reported by Nusbaum et al (11) who found a barium concentration of 30 $\mu\text{g} \cdot \text{g}^{-1}$ in samples of rib and calvarium. According to our measurements the barium concentration (archaeological weight) was constant along the fibula and the fingerbones.

SUMMARY AND CONCLUSION

The lead concentration in bones from archaeological Roman skeletons has been measured by non-destructive X-ray fluorescence analysis using the ratio between the number of Pb K X-rays and primary photons incoherently scattered at 90° . The bone mineral concentration was estimated from the ratio between the coherently and incoherently scattered photons. From these results, lead concentrations in fresh bone could be reconstructed using data from the literature for the ratio between mineral weight and fresh weight for various bones. The results from four skeletons show variations in lead concentration by a factor of four (based on fresh weight) between various bones in the skeleton. The results indicate that the average skeletal concentration may be estimated to within 50% from a single measurement of the finger phalanx.

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TABLE 1 LEAD CONCENTRATION $\mu\text{g}\cdot\text{g}^{-1}$

	PHALANX SHAFT	METACARPAL OR METATARSAL		FIBULA		RIB	SKULL	ESTIMATED AVERAGE SKELETAL CONC.	END/SHAFT		
		END	SHAFT	END	SHAFT				METACARPAL OR METATARSAL	FIBULA	
GRAVE 10 Male adult	unprepared archaeological bone estimated fresh weight conc.	198	268	149	230	174	423	195	-	1.80	1.32
		99	67	75	58	87	106	49	76	0.89	0.67
GRAVE 13 Female aged 25-35	unprepared archaeological bone estimated fresh weight conc.	501	1004	440	528	453	288	271	-	2.28	1.17
		251	251	220	132	227	72	68	146	1.14	0.58
GRAVE 14 Male aged 40-65	unprepared archaeological bone estimated fresh weight conc.	232	243	90	226	81	113	55	-	2.70	2.79
		116	61	45	57	41	28	14	35	1.35	1.39
GRAVE 35 Female aged 30-45	unprepared archaeological bone estimated fresh weight conc.	258	295	288	295	180	256	364	-	1.02	1.64
		129	74	144	74	90	64	91	86	0.51	0.82

Sample mass

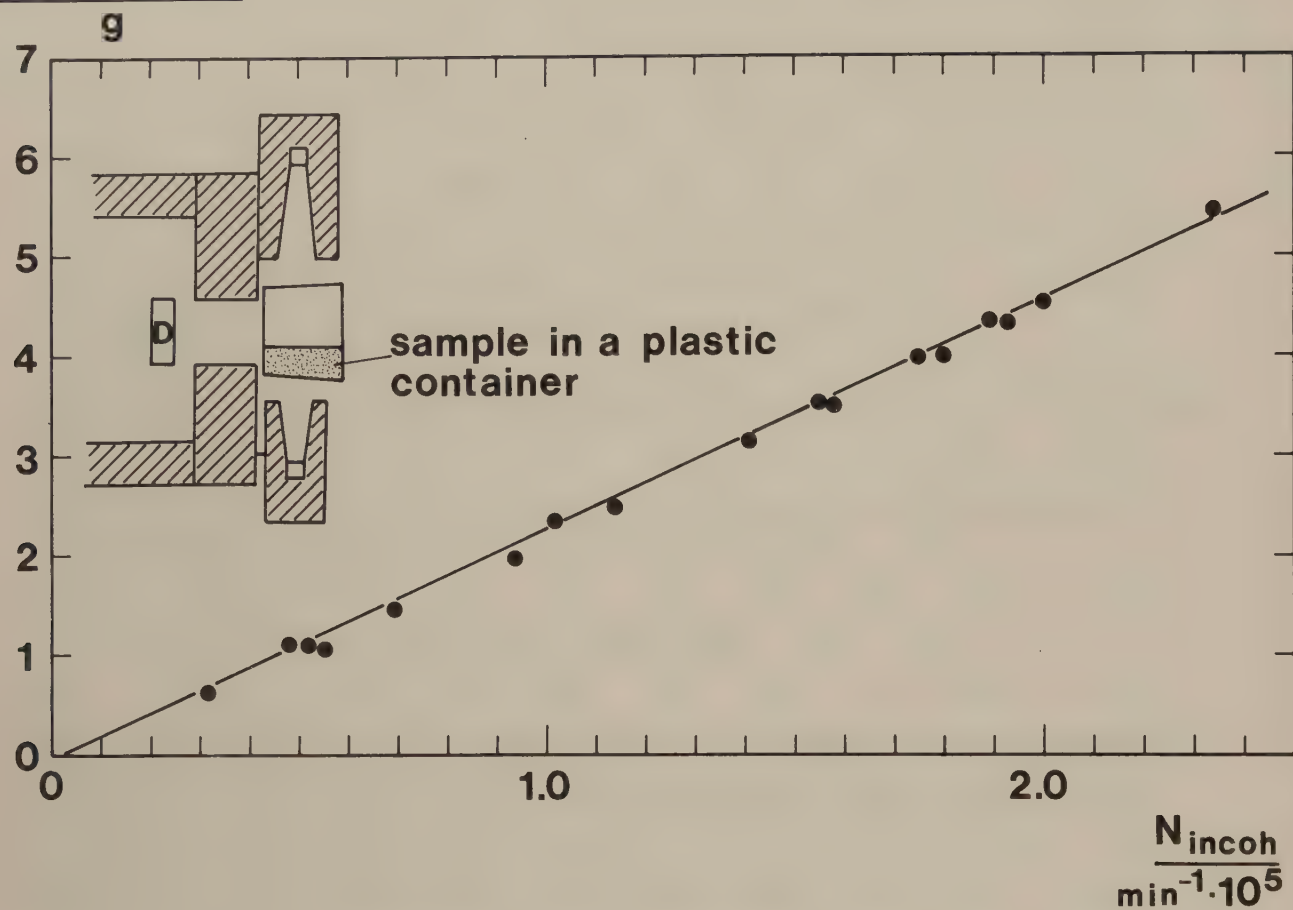


Figure 1 The count rate (N_{incoh}) of photons incoherently scattered in water samples of different masses.

$$\frac{N_{\text{Pb-K}\alpha}}{N_{\text{incoh}}} \cdot 10^{-5} \cdot (\mu\text{g}\cdot\text{g}^{-1})^{-1}$$

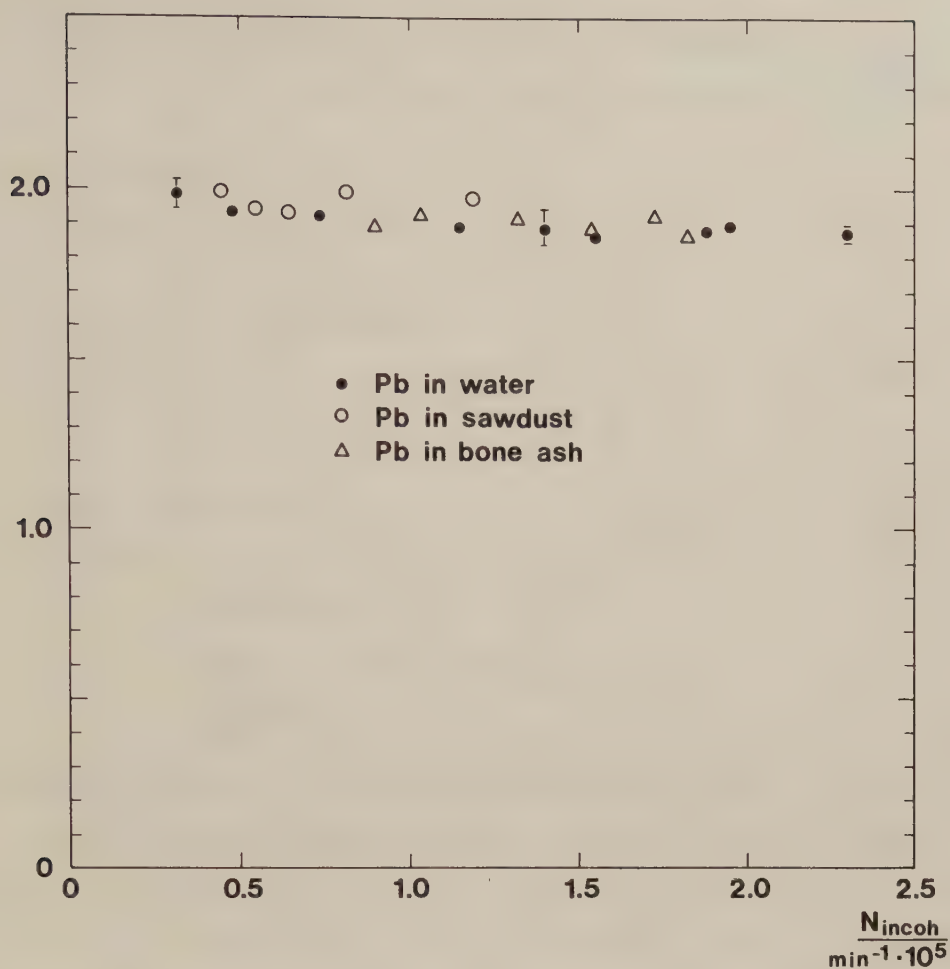


Figure 2 The ratio $(N_{\text{Pb-K}\alpha}/N_{\text{incoh}})$ between the count rate of lead characteristic X-rays and incoherently scattered photons from different samples with equal lead concentration.

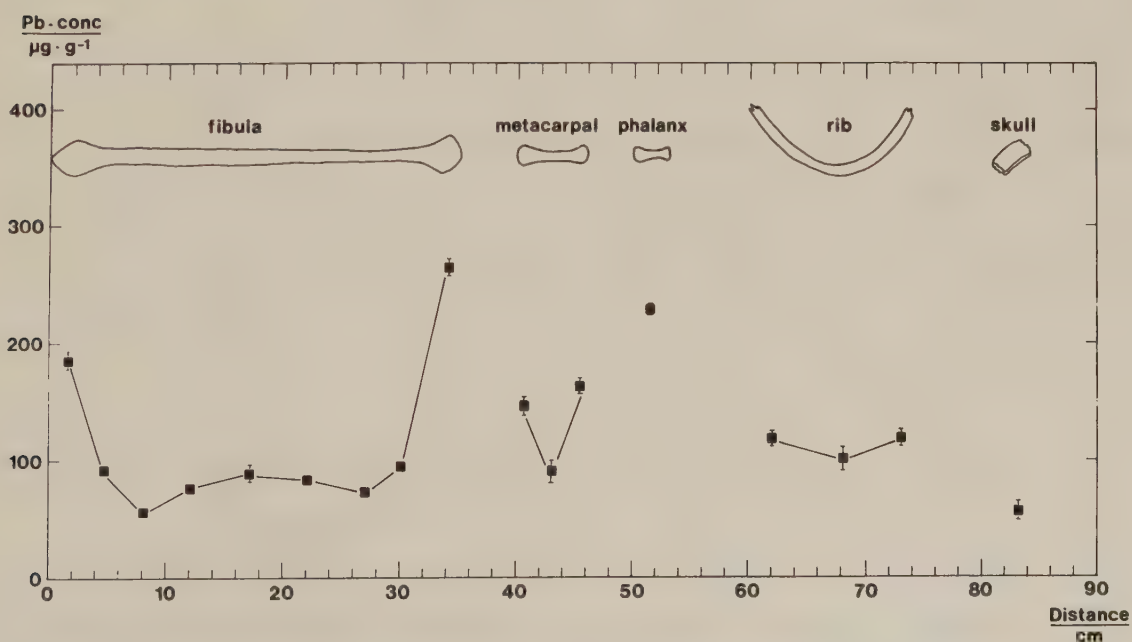


Figure 3 The lead concentration (per unit weight of untreated bone) in various bones from grave 14.

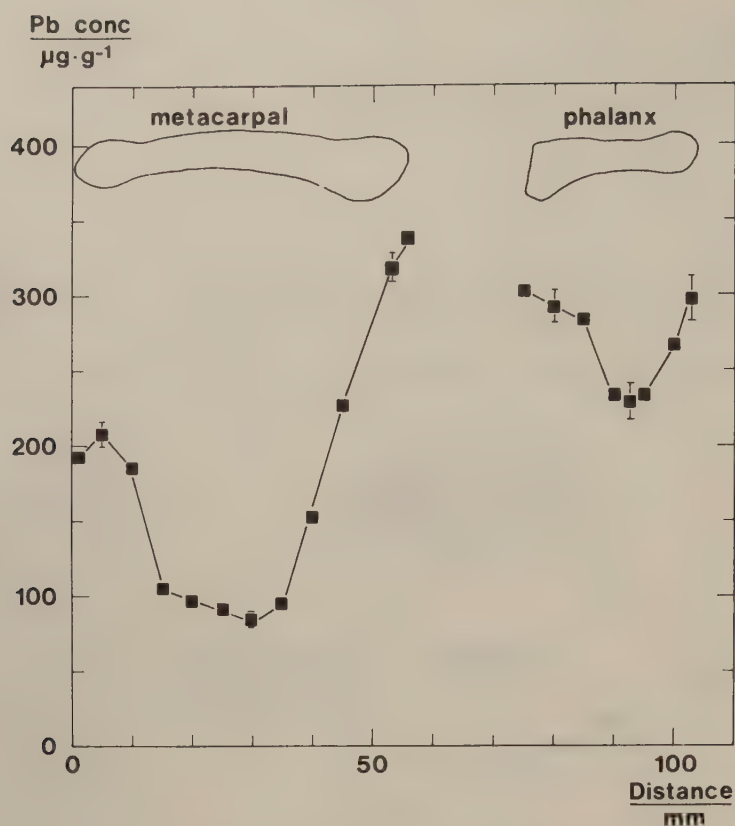


Figure 4 The lead concentration (per unit weight of untreated bone) along the metacarpal bone and the phalanx from grave 14.

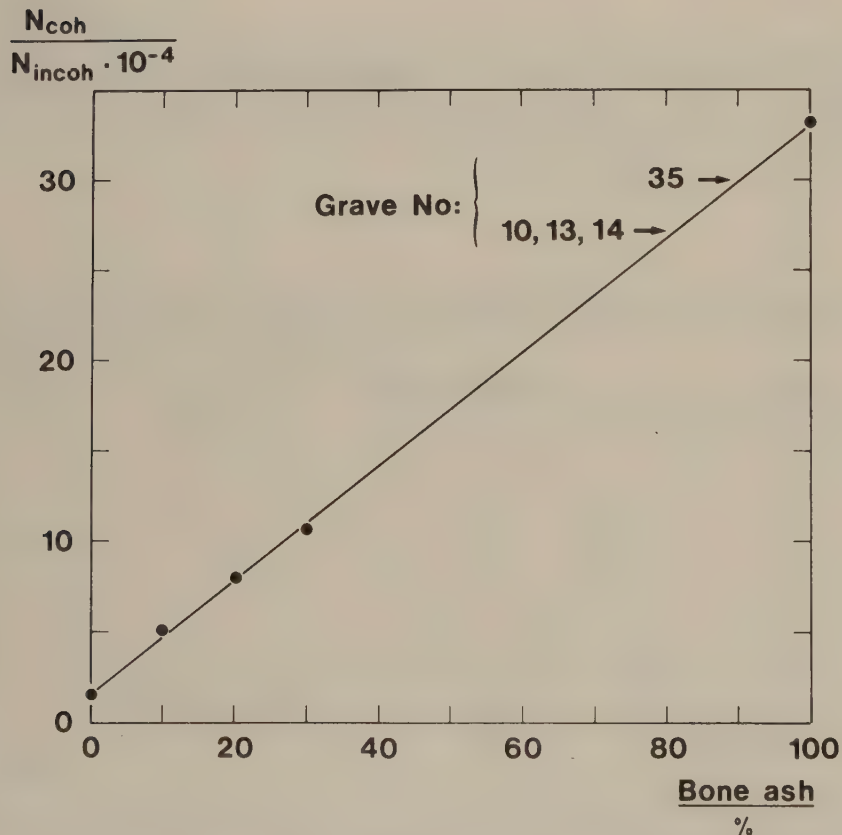


Figure 5 The ratio $(N_{\text{coh}}/N_{\text{incoh}})$ between the count rate of 90° coherent scattered 122 keV photons and 90° incoherently scattered 122 and 136 keV photons in soft tissue material mixed with known amounts of bone ash.

Cadmium in man measured in vivo by X-ray fluorescence analysis
(short title: Cadmium in man measured in vivo by X-ray fluorescence)

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ABSTRACT

The sensitivity and detection limit for measurements of the cadmium concentration in the kidney cortex of living man have been investigated using the X-ray fluorescence technique. A 11 GBq ^{241}Am -source is used to generate the characteristic K_{α} X-rays of cadmium. The variation of the sensitivity for detecting cadmium in various positions in a kidney has been studied.

Because of the pronounced variation in sensitivity with the depth in tissue, a selective measurement could be made in the kidney cortex. The minimum detectable Cd concentration varies between 20 and 40 $\mu\text{g}\cdot\text{g}^{-1}$ for distances between the skin and the kidney surface from 30 to 40 mm. The measured uncertainty of ± 3 mm in the distance between the skin and the kidney surface gives rise to an uncertainty of $\pm 30\%$ in the estimated Cd concentration. The mean absorbed dose to the kidney in the measurement is about 0.6 mGy. The X-ray fluorescence method is more advantageous than the alternative neutron capture gamma-ray analysis technique in so far as the total irradiation of the patient is concerned. The cadmium concentrations in the kidneys of five exposed persons were determined to lie between 30 and 143 $\mu\text{g}\cdot\text{g}^{-1}$.

1 INTRODUCTION

Cadmium is an important toxic environmental pollutant and represents an increasing health hazard to man (Friberg et al. 1974). In industrialized countries, all human beings will be exposed due to the diffuse spread of cadmium via food, water and air. For persons not exposed occupationally, intake from food and by inhaling cigarette smoke (Ellis et al. 1979) are the most important contributions to exposure. About 5% of the cadmium in the food intake is absorbed. This value can be higher if the person suffers from lack of calcium (Kjellström and Nordberg, 1978). When cadmium is inhaled, 10-40% is absorbed depending on the particle size of the cadmium dust (Friberg et al. 1974). For persons not exposed occupationally, the liver and the kidney (mainly the cortex) contain about 50% of the total body burden. In Sweden, the cadmium concentration in the kidney cortex is about $20 \mu\text{g}\cdot\text{g}^{-1}$ for smokers and $10 \mu\text{g}\cdot\text{g}^{-1}$ for non-smokers and about $1\mu\text{g}\cdot\text{g}^{-1}$ in the liver. The biological half life of cadmium in the kidney has been estimated to lie in the range 6-38 years (Kjellström and Nordberg, 1978, Elinder et al. 1976). For persons who have been heavily exposed to cadmium-containing dust or fume, concentrations of up to about $500 \mu\text{g}\cdot\text{g}^{-1}$ in the liver and in the kidney cortex have been reported (Friberg et al. 1974). When the exposure increases, a larger portion of the cadmium will be found in the liver (Kjellström and Nordberg, 1978). The correlation between the total body burden and the cadmium concentration in urine and blood is poor (Friberg et al. 1974). To estimate the total body burden, it is important to be able to measure directly the cadmium concentration in these organs which show the highest concentrations due to high uptake and/or slow excretion rates.

In vivo studies in the liver and in the kidney have hitherto been carried out in occupationally and non-occupationally exposed persons using neutron capture gamma ray analysis (Harvey et al. 1975, McLellan et al. 1975, Harvey et al. 1979, Roels et al. 1979, Thomas et al. 1979 and Ellis et al. 1979). A more detailed description of this method and its potential value for in vivo detection of cadmium has also been given (Vartsky et al. 1977). We have suggested the use of X-ray fluorescence analysis as an alternative method for cadmium detection in vivo (Ahlgren et al. 1980), using it in the same way as for in vivo analysis of lead (Ahlgren et al. 1976, Ahlgren and Mattsson, 1979, Ahlgren et al. 1979). In the present work, we have therefore studied the sensitivity and detection limit for cadmium in kidney and liver.

2 EXPERIMENTAL METHODS

Radiation from ^{241}Am was used to generate the characteristic X-rays of cadmium ($K_{\alpha 1,2} = 23.1 \text{ keV}$). A disc-shaped 11 GBq source (12 mm diameter) was used to measure the cadmium concentration in the kidney in a measuring geometry with $90-110^\circ$ between the primary and measured radiation. An annular-shaped 11 GBq source (34 mm diameter) was used for measurements on the liver in a measuring geometry with 180° between the primary and measured radiation. In addition to the 59.5 keV γ -rays (36% per disintegration), the ^{241}Am source also emits 26.3 keV γ -rays (3%) and characteristic X-rays between 34 and 40 keV from cerium in the source capsule. Most of these low energy photons will be absorbed before they reach the kidney or the liver and will therefore only contribute with scattered radiation which can interfere with the registration of the characteristic X-rays of cadmium. A 26 keV photon which is Compton scattered through 90° will have an energy quite close to those of cadmium K_{α} X-rays. The fluence of low energy photons has therefore been reduced by placing a 70 μm Mo filter in front of the source. This also simplifies the subtraction of background below the cadmium K_{α} X-ray peak.

The secondary radiation from the irradiated volume was studied with a Ge(Li)-detector (16 mm diameter, 5.2 mm thick, energy resolution 450 eV FWHM at 23 keV, 0.13 mm Be window). The relative sensitivity for cadmium detection was studied with a "point" source of Cd Cl_2 (35 mm^3) placed at different positions in a water-filled phantom. The position of the detector and the radiation source was fixed as shown in figure 3. The absolute sensitivity and the detection limit for cadmium detection were studied with kidney and liver phantoms placed at different positions in a water-filled body-phantom. The kidney phantom was made of a thin-walled (2 mm) perspex cylinder (height 110 mm, inner diameter 40 mm) and the liver was simulated by a thin-walled perspex parallelepiped with dimensions 150 x 150 x 60 mm^3 . These phantoms were filled with solutions of cadmium of various known concentrations. In order to optimize the geometrical arrangements, the effect of using different designs of collimator between the radiation source and detector was investigated.

The absorbed dose rate at different positions in the water phantom was measured with small (2 x 2 x 1 mm^3) extruded LiF dosimeters. The mean absorbed dose in the kidney and the energy imparted were then calculated. Finally, we have used the technique for in vivo measurements on 5 persons

who had been exposed to cadmium for periods between 6 and 25 years. These measurements were carried out on the right kidney with the person sitting upright. The measuring geometry is shown in figure 1. The detector is located at the back of the person measured. In order to get the shortest distance between the skin and the kidney, the angle between the primary and measured radiation was chosen to be 110° . The position of the kidney and its depth in the body were measured with a B-scan ultrasonic technique. This localisation was carried out with the subjects in the same position as in the cadmium determinations. The detector and radiation source were directed towards a point 10 mm inside the kidney surface with the collimators close to the skin. For two persons, the ultrasonic measurement was carried out both before and after the cadmium measurement.

3 RESULT AND DISCUSSION

Figure 1 shows the measuring geometry and the pulse-height distribution from a measurement of the cadmium concentration in the kidney of an occupationally exposed person. The pulse-height distribution is dominated by those of the 59.6 keV photons which are incoherently scattered in the body and then registered in the detector. With an angle of 110° between the primary and the measured radiation as in figure 1, the "compton peak" is located at about 52 keV. With an angle of 180° , it will be located at about 49 keV, but does still not interfere with the cadmium X-rays (23 keV). The width of the distribution of the compton scattered photons increases with an increasing opening angle of the collimators in front of the detector and the radiation source.

The background on which the characteristic X-rays of cadmium are registered in the pulse-height distribution is due to photons which are multiply scattered mainly in the investigated volume. The collimators in front of the detector and the radiation source were therefore designed to cut out contributions from these parts of the body which do not contain cadmium. The best detection limit was found using an elliptically shaped collimator permitting irradiation of an elliptical area in the centre of the kidney. At a depth of 4 cm, about half the length of the kidney was irradiated, the axes of the ellipse being 40 and 50 mm respectively. Figure 2 shows how the relative sensitivity for cadmium detection using X-ray fluorescence analysis depends on the depth in tissue for two different geometries. For comparison, the rela-

tive sensitivity for neutron capture gamma ray analysis is also given (Vartsky et al. 1977). The pronounced variation in sensitivity with depth for the X-ray fluorescence technique is due mainly to the varying fluence of primary photons and the varying solid angle of the detector due to the small distances between the radiation source, the sample and the detector. It also depends on the attenuation of the primary photons ($\mu = 0.20 \text{ cm}^{-1}$) and of the cadmium K_{α} X-rays ($\mu = 0.61 \text{ cm}^{-1}$). Figure 2 and 3 show that the maximum variation in sensitivity within a kidney of 40 mm diameter is a factor of 30 for the 90° geometry. When using the 180° geometry, the factor becomes 180. This pronounced dependence on depth means that the measurements reflect the cadmium concentration in the kidney cortex rather than in the whole kidney. To be able to calculate the absolute cadmium concentration, the distance between the skin and the kidney surface must be carefully measured. This was done with a B-scan ultrasonic measurement. Repeated determinations of the depth of the right kidney in one of the authors were carried out in the same conditions as for the persons studied. The distance between the skin and the nearest kidney surface was determined to be $\{45.7 \pm 0.9 \text{ (S.D.)}\}$ mm, i.e., a relative standard deviation of 2.1%. The uncertainty in the effective distance between the skin and the kidney surface was estimated to be ± 3 mm. The sensitivity for neutron capture gamma ray analysis is almost independent of the depth of the kidney in the body and of the distribution of the cadmium in the organ because of the uniform neutron fluence in the body and the high penetration of the 559 keV γ -rays measured.

The detection limit for the X-ray fluorescence method given in figure 4 corresponds to the number of registrations in the Cd K_{α} X-ray peak needed to be 3 standard deviations above background after 30 min measuring time. Using the 90° geometry, the detection limit for cadmium is $20 \mu\text{g} \cdot \text{g}^{-1}$ when the kidney surface is 30 mm below the skin and $40 \mu\text{g} \cdot \text{g}^{-1}$ when the distance is 40 mm. Corresponding value for liver measurements using the 180° geometry are $30 \mu\text{g} \cdot \text{g}^{-1}$ and $80 \mu\text{g} \cdot \text{g}^{-1}$. The 90° geometry gives the best detectability since this geometry has the highest sensitivity and the lowest background count rate in the Cd K_{α} region. Using 180° between the primary and measured radiations, the adjustment of the detector and radiation source towards the cadmium containing organ is easier to carry out since the detector and radiation source are mounted in one unit. To minimize the amount of scattered radiation from that part of the body which is closest to the detector, the collimator in front of the radiation source is designed to irradiate that part of the body which is located deeper

than 1 cm.

The absorbed dose to the skin was 4.5 mGy (450 mrad) and the absorbed dose to the kidney varied between 1.2 and 0.3 mGy (mean value 0.55 mGy) after 30 minutes irradiation with the kidney surface 3 cm below the skin. In table 1, the absorbed dose and the energy imparted for this technique are compared with the corresponding value for the neutron capture gamma ray analysis technique for in vivo cadmium detection. As seen from table 1, the absorbed dose to the kidney after an X-ray fluorescence measurement is of the same magnitude as that from an ordinary X-ray examination of the kidney. When the risk associated with a certain diagnostic radiological investigation is to be estimated, the energy imparted is a more relevant quantity than the absorbed dose. Since the radiation field is only about 3 cm^2 at the skin, the total energy imparted for an X-ray fluorescence measurement is only about 0.4 mJ. Using the neutron capture gamma ray technique, the energy imparted will be considerably larger due to the large neutron field (260 cm^2) at the skin. A common X-ray examination of the kidneys (urography) gives an energy imparted of around 240 mJ.

Since we have demonstrated that the technique has a sufficiently high sensitivity and because there were no objections against it from the ethical point of view, the new technique for in vivo determination of cadmium described here was, as earlier mentioned, used for measurements of 5 occupationally exposed persons. Figure 1 shows the result of one such measurement of a patient's right kidney. To relate the count rate in the Cd K_{α} peak to the cadmium concentration in the kidney cortex, measurements on the cylindrical kidney phantom filled by solutions of known cadmium concentration (30, 300 and 1000 $\mu\text{g/g}$) were carried out. The kidney phantom was placed in the water phantom at the same position relative to the radiation source and the detector as in the actual in vivo measurement. The uncertainty in the measured distance between the skin and kidney cortex was earlier estimated to be $\pm 3 \text{ mm}$, giving rise to an uncertainty in the calculated cadmium concentration of $\pm 30\%$. Figure 5 shows the results of the in vivo measurements together with the expected cadmium concentration in normals and cadmium exposed persons. In table 2, the cadmium concentration in blood and urine on the day of measurement is also given as well as the person's period of exposure. For two of the subjects, the measured cadmium concentration in the kidney cortex was within the normal range and for the other 3 the cadmium concentration

was within the range reported for occupationally exposed persons. With one exception, the cadmium concentration increased with the period of exposure.

4 CONCLUSIONS

The method proposed in this work gives the possibility for in vivo determinations of cadmium in the kidneys of occupationally exposed persons as well as in sections of the normal population. In comparison with the alternative neutron capture gamma ray analysis technique, the X-ray fluorescence method is more favourable in so far as the irradiation of the patient is concerned. Because of the pronounced variation of sensitivity with depth in tissue, a selective measurement of the kidney cortex, which is the interesting part, can be made. The X-ray fluorescence equipment can easily be moved to factories and hospitals where the measurements can be performed, provided that a careful localization of the kidney has earlier been carried out.

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Table 1 Mean absorbed dose and energy imparted in in vivo determination of Cd.

Type of investigation	Mean absorbed kidney dose mGy	Energy imparted mJ
XRF of cadmium in a kidney	0.6	0.4
Prompt gamma neutron activation analysis of cadmium in a kidney	0.57 ¹⁾ (neutrons)	1.6 ^{x)} , ^{xx)}
	0.29 ¹⁾ (photons)	0.9 ^{x)} , ^{xx)}
Urography	3.3 ²⁾	240 ²⁾

x) Estimated by the authors

xx) The biological effects of the energy imparted by neutrons at low absorbed doses may be 10-100 times larger than that of the same energy imparted by photons (Rossi, 1977)

1) Vartsky et al. 1977

2) Carlsson, 1965

Table 2 Measured cadmium concentration in persons who have used cadmium containing solders.

Person nr	Age	Exposure period	Cd-concentration		
	year	year	kidney cortex xx)	blood µg/l	urine µg/l
1	35	14	143±45	3.3	4.4
2	64	30	36±13	7.0	13.8
3	54	25	137±42	x	x
4	35	10	47±17	x	x
5	33	6	30±22	x	x

x) not yet analysed

xx) the uncertainty indicated is 1 SD (due to counting statistics and the estimated uncertainty in the kidney position).

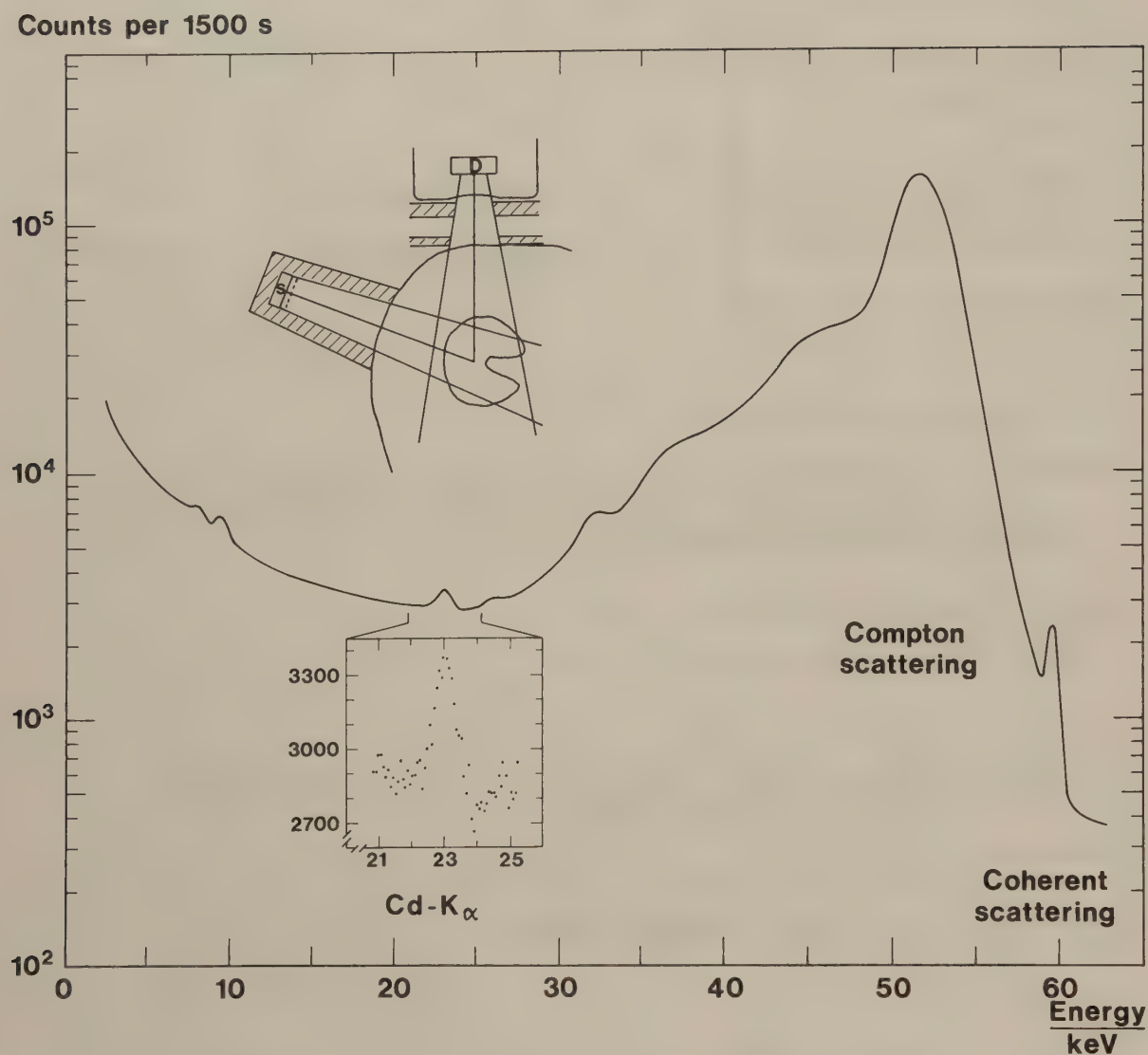


Figure 1

Pulse height distribution from a 16 mm (diam) x 5.2 mm Ge(Li)-detector (D) looking at the right kidney irradiated by a 11 GBq Am-241 source (S) in the geometry indicated in the figure. From this in vivo measurement, the Cd-concentration in the kidney (cortex) of this occupationally exposed person was estimated to be 137 $\mu\text{g}\cdot\text{g}^{-1}$.

Relative sensitivity for Cd-detection

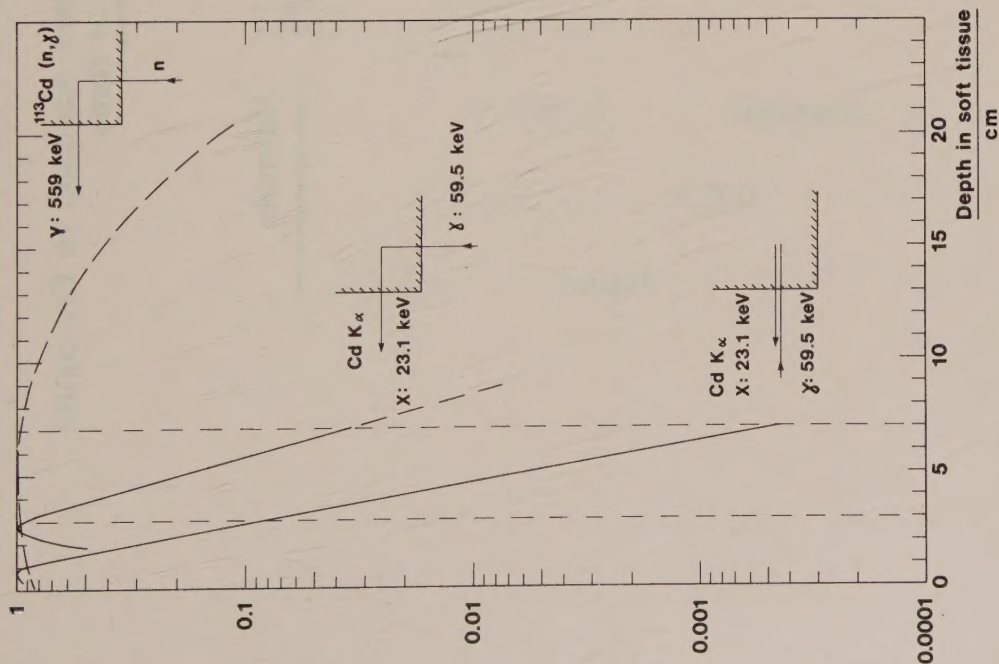


Figure 2

Relative sensitivity for Cd- detection along the central axis of the detector at various depths in a water phantom. The corresponding results for neutron capture gamma ray analysis (Vartsky et al. 1977) are also given. The extension of a kidney is indicated in the figure.

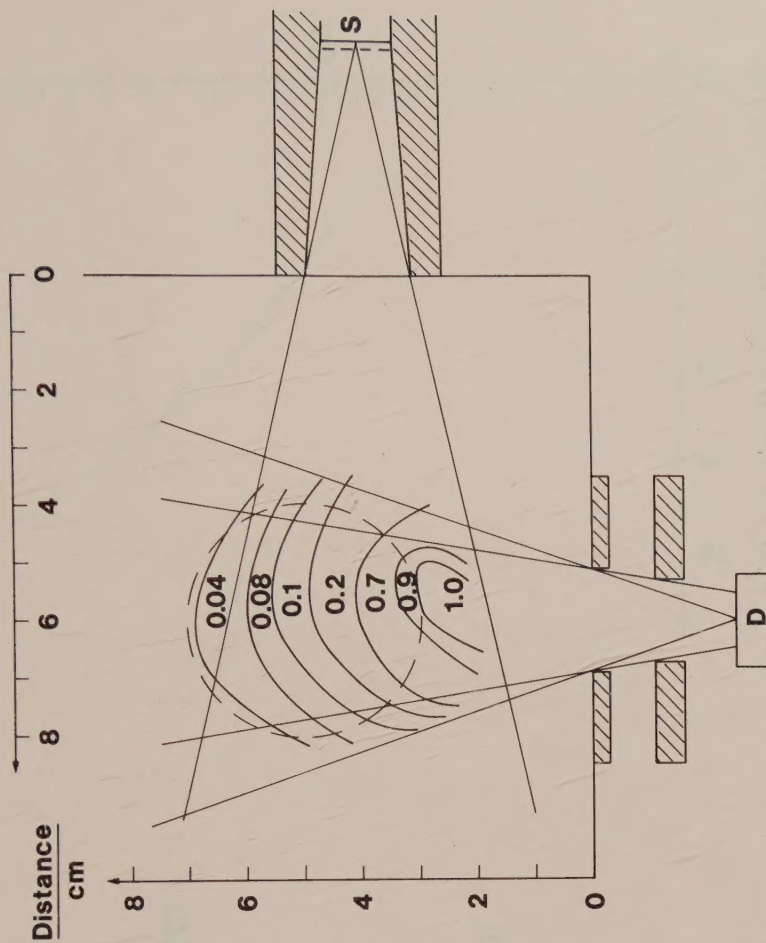


Figure 3

Relative iso-sensitivity curves for Cd-detection in water in a plane through the central axes of the detector and the source.

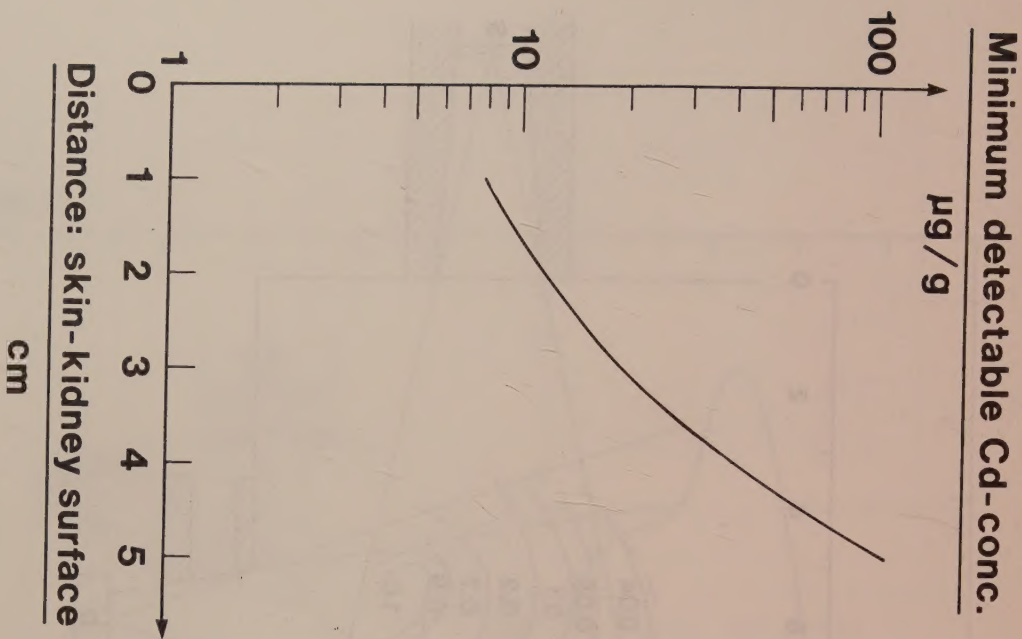


Figure 4

The minimum detectable Cd-concentration in the renal cortex for various distances between the skin and the kidney surface. The levels at which meaningful determinations of the Cd-concentration can be made is about twice the minimum detectable concentration.

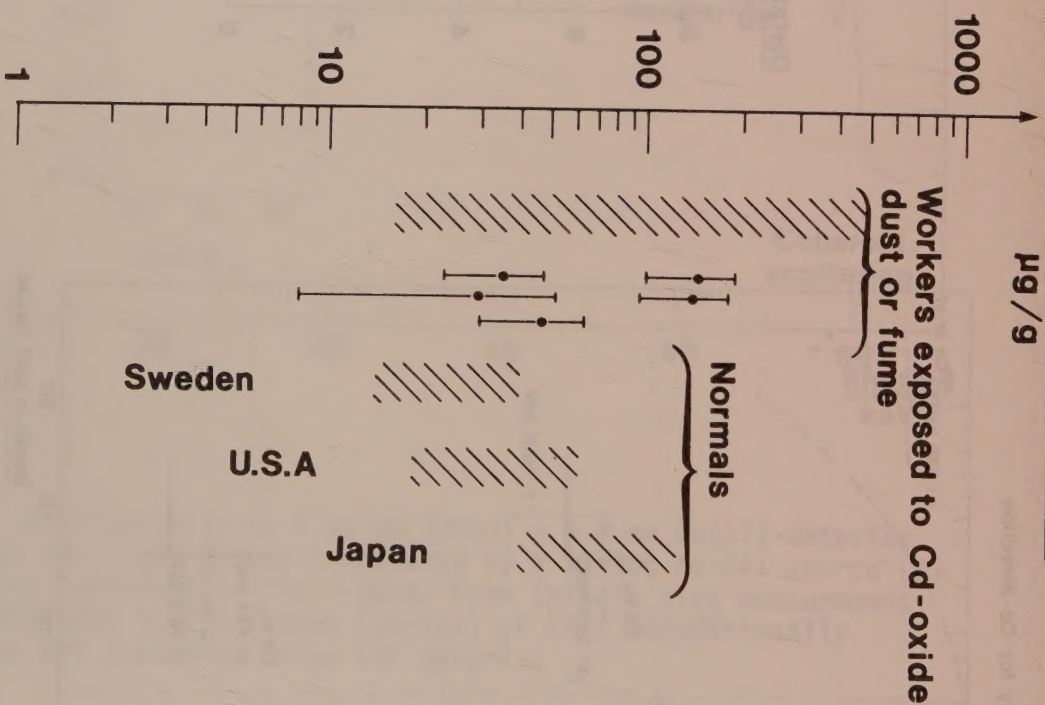


Figure 5

The results of our *in vivo* measurements of Cd in human kidneys are compared with reported concentrations of Cd in the renal cortices of occupationally exposed persons and normals as measured in biopsy or autopsy samples (Friberg et al. 1974). The uncertainty indicated is 1 SD (due to counting statistics and the estimated uncertainty in the kidney position).

